WEBVTT

NOTE duration:"01:00:42.2400000"

NOTE recognizability:0.826

NOTE language:en-us

NOTE Confidence: 0.757621294166667

00:00:00.000 --> 00:00:02.982 Everybody or we are very fortunate

NOTE Confidence: 0.757621294166667

00:00:02.982 --> 00:00:06.240 today to have doctor Haluska here.

NOTE Confidence: 0.757621294166667

00:00:06.240 --> 00:00:09.672 Doctor Haluska is professor of John

NOTE Confidence: 0.757621294166667

00:00:09.672 --> 00:00:12.757 Hopkins and current chairman of

NOTE Confidence: 0.757621294166667

00:00:12.757 --> 00:00:15.549 Society of Cardiovascular Pathology.

NOTE Confidence: 0.757621294166667

00:00:15.550 --> 00:00:16.750 So I look at his CV,

NOTE Confidence: 0.757621294166667

00:00:16.750 --> 00:00:17.926 I look at that, my God,

NOTE Confidence: 0.757621294166667

00:00:17.930 --> 00:00:20.874 it's it's a really good example of

NOTE Confidence: 0.757621294166667

00:00:20.874 --> 00:00:23.598 academic pathologist can read that he

NOTE Confidence: 0.757621294166667

00:00:23.598 --> 00:00:26.566 graduated from Big Forest and did his

NOTE Confidence: 0.757621294166667

00:00:26.566 --> 00:00:29.906 AP and Fellowship at Johns Hopkins.

NOTE Confidence: 0.757621294166667

00:00:29.910 --> 00:00:31.122 For the diagnostic part,

NOTE Confidence: 0.757621294166667

00:00:31.122 --> 00:00:33.811 I think a lot of people have joined

NOTE Confidence: 0.757621294166667

00:00:33.811 --> 00:00:36.223 this diagnostic meeting in the morning,

NOTE Confidence: 0.757621294166667

00:00:36.230 --> 00:00:39.280 right is internationally well known

NOTE Confidence: 0.757621294166667

00:00:39.280 --> 00:00:41.720 cardiovascular pathologist not only

NOTE Confidence: 0.757621294166667

00:00:41.720 --> 00:00:45.110 practice in John Hopkins but also have

NOTE Confidence: 0.757621294166667

00:00:45.110 --> 00:00:47.336 consulting service from local hospital

NOTE Confidence: 0.757621294166667

00:00:47.336 --> 00:00:51.390 and also as far as from Texas, Texas.

NOTE Confidence: 0.757621294166667

00:00:51.390 --> 00:00:54.174 So as the investigator,

NOTE Confidence: 0.757621294166667

00:00:54.174 --> 00:00:59.008 he published 220 publications including

NOTE Confidence: 0.8352534275

00:00:59.530 --> 00:01:01.558 reviews and Case report

NOTE Confidence: 0.806599880833333

00:01:01.910 --> 00:01:05.144 and he is an internationally well

NOTE Confidence: 0.806599880833333

00:01:05.144 --> 00:01:08.310 known investigator for my micro RNA,

NOTE Confidence: 0.806599880833333

00:01:08.310 --> 00:01:12.830 especially related to cardiovascular disease.

NOTE Confidence: 0.806599880833333

00:01:12.830 --> 00:01:17.186 His current research are supported by two

NOTE Confidence: 0.806599880833333

00:01:17.190 --> 00:01:22.486 R1SP I and three Co investigator R1 Grant.

NOTE Confidence: 0.806599880833333

00:01:22.490 --> 00:01:25.745 As at the educator, the the course

NOTE Confidence: 0.806599880833333

00:01:25.745 --> 00:01:28.610 director for the medical school,

NOTE Confidence: 0.806599880833333

00:01:28.610 --> 00:01:31.842 cost director for postgraduate,

NOTE Confidence: 0.806599880833333

00:01:31.842 --> 00:01:34.266 Fellows and resident.

NOTE Confidence: 0.806599880833333

00:01:34.270 --> 00:01:37.680 Anymore too much.

NOTE Confidence: 0.806599880833333

00:01:37.680 --> 00:01:41.795 He is the he had the frequently speaker

NOTE Confidence: 0.806599880833333

00:01:41.795 --> 00:01:44.660 at national and international meetings

NOTE Confidence: 0.806599880833333

00:01:44.746 --> 00:01:48.507 and organize several sessions in the USAP.

NOTE Confidence: 0.806599880833333

00:01:48.507 --> 00:01:54.323 And one thing he mentored about 40 trainees.

NOTE Confidence: 0.806599880833333

00:01:54.330 --> 00:01:55.790 Couple of them already showed

NOTE Confidence: 0.806599880833333

00:01:55.790 --> 00:01:59.128 their professor John Hopkins now.

NOTE Confidence: 0.806599880833333

00:01:59.130 --> 00:02:02.203 One thing I think not very classical

NOTE Confidence: 0.806599880833333

00:02:02.203 --> 00:02:04.550 typical of academic pathologist,

NOTE Confidence: 0.806599880833333

00:02:04.550 --> 00:02:07.693 he has a full patent and invention

NOTE Confidence: 0.806599880833333

00:02:07.693 --> 00:02:10.858 and he still have the potential

NOTE Confidence: 0.7388189675

00:02:10.870 --> 00:02:15.170 to be building there. Yeah. Thank you.

NOTE Confidence: 0.880635388181818

00:02:15.760 --> 00:02:17.124 Thank you, Peter. Well,

NOTE Confidence: 0.880635388181818

00:02:17.124 --> 00:02:19.420 thank you very much for inviting me.

NOTE Confidence: 0.880635388181818

00:02:19.420 --> 00:02:20.860 Only 1/4 of what Peter

NOTE Confidence: 0.880635388181818

00:02:20.860 --> 00:02:22.300 said about me was right.

NOTE Confidence: 0.880635388181818

00:02:22.300 --> 00:02:23.458 I won't tell you which quarter,

NOTE Confidence: 0.880635388181818

00:02:23.460 --> 00:02:26.420 but not the impressive stuff I'm certain of.

NOTE Confidence: 0.880635388181818

00:02:26.420 --> 00:02:29.220 It is an absolute pleasure to be here.

NOTE Confidence: 0.880635388181818

00:02:29.220 --> 00:02:32.889 At Yale, yes.

NOTE Confidence: 0.880635388181818

00:02:32.890 --> 00:02:34.530 I do not know how to turn the chime off.

NOTE Confidence: 0.647799262

00:02:35.330 --> 00:02:39.310 Do you know? Currently, apparently.

NOTE Confidence: 0.706623653333333

00:02:39.580 --> 00:02:41.596 OK, I don't wanna disrupt anything.

NOTE Confidence: 0.749212409

00:02:45.930 --> 00:02:47.120 And I'm sure that's the sound of

NOTE Confidence: 0.749212409

00:02:47.120 --> 00:02:48.353 people coming on, which is fine.

NOTE Confidence: 0.749212409

00:02:48.353 --> 00:02:49.799 I I will know sort of.

NOTE Confidence: 0.749212409

00:02:49.800 --> 00:02:51.303 At my wedding we had a video at the

NOTE Confidence: 0.749212409

00:02:51.303 --> 00:02:52.896 end and I saw a guy walking on the

NOTE Confidence: 0.749212409

00:02:52.896 --> 00:02:54.543 video and the last two minutes of the

NOTE Confidence: 0.749212409

00:02:54.543 --> 00:02:56.136 wedding he missed the whole thing,

NOTE Confidence: 0.749212409

00:02:56.136 --> 00:02:58.747 but we we documented that he showed

NOTE Confidence: 0.749212409

00:02:58.747 --> 00:03:01.598 up late and our wedding started on

NOTE Confidence: 0.749212409

00:03:01.598 --> 00:03:03.640 time just like today, which is great.

NOTE Confidence: 0.861866645555556

00:03:05.970 --> 00:03:07.986 I I don't know if you're gonna find that.

NOTE Confidence: 0.881450133333333

00:03:11.350 --> 00:03:13.066 It's not going to bother me.

NOTE Confidence: 0.881450133333333

00:03:13.070 --> 00:03:15.700 Then you can bring up.

NOTE Confidence: 0.881450133333333

00:03:15.700 --> 00:03:16.960 Yes, Sir, I'm. That's where I am.

NOTE Confidence: 0.65727773

00:03:18.500 --> 00:03:24.820 This, yeah. Adopted. It's not here yet.

NOTE Confidence: 0.7465352725

00:03:26.910 --> 00:03:27.930 Nope, doesn't give me

NOTE Confidence: 0.809751363333333

00:03:27.940 --> 00:03:29.732 that option. That's where

NOTE Confidence: 0.809751363333333

00:03:29.732 --> 00:03:31.299 I am. Very long time.

NOTE Confidence: 0.015140802

00:03:36.710 --> 00:03:37.730 Recipients.

NOTE Confidence: 0.884970118

00:03:49.490 --> 00:03:51.614 I think now everybody has, everyone has

NOTE Confidence: 0.884970118

00:03:51.614 --> 00:03:53.550 used these extra few minutes to join us.

NOTE Confidence: 0.884970118

00:03:53.550 --> 00:03:55.290 I don't think we'll be hearing

NOTE Confidence: 0.884970118

00:03:55.290 --> 00:03:56.450 the ringing much more.

NOTE Confidence: 0.884970118

00:03:56.450 --> 00:03:58.277 So I want to again thank you so much

NOTE Confidence: 0.884970118

00:03:58.277 --> 00:04:00.267 for inviting me to come to Yale today.

NOTE Confidence: 0.884970118

00:04:00.270 --> 00:04:02.646 It is an absolute pleasure to be here.

NOTE Confidence: 0.884970118

00:04:02.650 --> 00:04:05.188 For those of you who are watching as well,

NOTE Confidence: 0.884970118

00:04:05.190 --> 00:04:07.080 it's nice to see you all remotely.

NOTE Confidence: 0.884970118

00:04:07.080 --> 00:04:09.678 I'm going to be talking about

NOTE Confidence: 0.884970118

00:04:09.678 --> 00:04:10.977 diagnosing myocarditis challenges.

NOTE Confidence: 0.884970118

00:04:10.980 --> 00:04:13.600 And opportunities.

NOTE Confidence: 0.884970118

00:04:13.600 --> 00:04:16.218 Should I get this to move forward?

NOTE Confidence: 0.884970118

00:04:16.220 --> 00:04:17.088 And I should say,

NOTE Confidence: 0.884970118

00:04:17.088 --> 00:04:18.710 for the first time in my life,

NOTE Confidence: 0.884970118

00:04:18.710 --> 00:04:20.170 I actually have a disclosure.

NOTE Confidence: 0.884970118

00:04:20.170 --> 00:04:22.368 I just started consulting for a company.

NOTE Confidence: 0.884970118

00:04:22.370 --> 00:04:23.528 I haven't gotten a dime yet,

NOTE Confidence: 0.884970118

00:04:23.530 --> 00:04:25.570 but I'm awfully excited about the

NOTE Confidence: 0.884970118

00:04:25.570 --> 00:04:27.484 possibility of that happening and I

NOTE Confidence: 0.884970118

00:04:27.484 --> 00:04:29.206 needed to share that with you here.

NOTE Confidence: 0.884970118

00:04:29.210 --> 00:04:30.788 So I have a few objectives.

NOTE Confidence: 0.884970118

00:04:30.790 --> 00:04:32.986 They are to recognize the challenges

NOTE Confidence: 0.884970118

00:04:32.986 --> 00:04:35.130 in making a myocarditis diagnosis,

NOTE Confidence: 0.884970118

00:04:35.130 --> 00:04:37.050 explain why that challenge causes

NOTE Confidence: 0.884970118

00:04:37.050 --> 00:04:38.970 difficulties in the general population,

NOTE Confidence: 0.884970118

00:04:38.970 --> 00:04:41.388 and learn about new directions to

NOTE Confidence: 0.884970118

00:04:41.388 --> 00:04:43.000 improve the myocarditis diagnosis

NOTE Confidence: 0.884970118

00:04:43.065 --> 00:04:44.509 that we are undertaking.

NOTE Confidence: 0.884970118

00:04:44.510 --> 00:04:45.658 And this is what I'm going to

NOTE Confidence: 0.884970118

00:04:45.658 --> 00:04:46.470 try and talk to you.

NOTE Confidence: 0.884970118

00:04:46.470 --> 00:04:47.040 About today,

NOTE Confidence: 0.884970118

00:04:47.040 --> 00:04:49.035 I'll keep coming back to this slide,

NOTE Confidence: 0.884970118

00:04:49.040 --> 00:04:50.504 which is of course I want to give

NOTE Confidence: 0.884970118

00:04:50.504 --> 00:04:52.138 you a little bit of information

NOTE Confidence: 0.884970118

00:04:52.138 --> 00:04:53.358 about what is myocarditis.

NOTE Confidence: 0.884970118

00:04:53.360 --> 00:04:55.390 Then talk about different ways

NOTE Confidence: 0.884970118

00:04:55.390 --> 00:04:57.014 that myocarditis is diagnosed.

NOTE Confidence: 0.884970118

00:04:57.020 --> 00:04:58.495 Spend some time talking about

NOTE Confidence: 0.884970118

00:04:58.495 --> 00:04:59.380 the Dallas criteria,

NOTE Confidence: 0.884970118

00:04:59.380 --> 00:05:02.124 which is what we use in Histology and

NOTE Confidence: 0.884970118

00:05:02.124 --> 00:05:05.196 then our our attempts to revise the

NOTE Confidence: 0.884970118

00:05:05.196 --> 00:05:07.506 Dallas criteria and then diagnosing

NOTE Confidence: 0.884970118

00:05:07.585 --> 00:05:10.270 myocarditis beyond the immune cells.

NOTE Confidence: 0.884970118

00:05:10.270 --> 00:05:12.442 So let's start with a straightforward

NOTE Confidence: 0.884970118

00:05:12.442 --> 00:05:13.528 definition of myocarditis.

NOTE Confidence: 0.884970118

00:05:13.530 --> 00:05:15.220 This is inflammation of the

NOTE Confidence: 0.884970118

00:05:15.220 --> 00:05:16.572 heart with myocyte injury.

NOTE Confidence: 0.884970118

00:05:16.580 --> 00:05:18.603 And we have a couple of Histology

NOTE Confidence: 0.884970118

00:05:18.603 --> 00:05:20.302 slides showing this classic pattern

NOTE Confidence: 0.884970118

00:05:20.302 --> 00:05:22.247 of a inflammatory cell infiltrate.

NOTE Confidence: 0.884970118

00:05:22.250 --> 00:05:24.343 This happens to be a number of

NOTE Confidence: 0.884970118

00:05:24.343 --> 00:05:26.190 lymphocytes and some myocyte injury,

NOTE Confidence: 0.884970118

00:05:26.190 --> 00:05:28.654 both at a lower power and a

NOTE Confidence: 0.884970118

00:05:28.654 --> 00:05:30.364 higher power showing a number

NOTE Confidence: 0.884970118

00:05:30.364 --> 00:05:31.820 of these infiltrating cells.

NOTE Confidence: 0.884970118

00:05:31.820 --> 00:05:34.046 So that's a very straightforward definition.

NOTE Confidence: 0.884970118

00:05:34.050 --> 00:05:36.842 There are a number of causes of myocarditis

NOTE Confidence: 0.884970118

00:05:36.842 --> 00:05:39.188 that some of these are infectious.

NOTE Confidence: 0.884970118

00:05:39.190 --> 00:05:41.318 We have a number of different viruses.

NOTE Confidence: 0.884970118

00:05:41.320 --> 00:05:44.180 That are associated with myocarditis,

NOTE Confidence: 0.884970118

00:05:44.180 --> 00:05:45.392 viral myocarditis and that's

NOTE Confidence: 0.884970118

00:05:45.392 --> 00:05:47.580 something we can test for by PCR

NOTE Confidence: 0.884970118

00:05:47.580 --> 00:05:48.836 sometimes identify what these

NOTE Confidence: 0.884970118

00:05:48.836 --> 00:05:51.127 viruses are and type them a number

NOTE Confidence: 0.884970118

00:05:51.127 --> 00:05:52.797 of parasites can cause myocarditis.

NOTE Confidence: 0.884970118

00:05:52.800 --> 00:05:54.473 I brought up Lyme disease because I

NOTE Confidence: 0.884970118

00:05:54.473 --> 00:05:56.126 am here excited to be in Connecticut

NOTE Confidence: 0.884970118

00:05:56.126 --> 00:05:57.014 to give the talk.

NOTE Confidence: 0.884970118

00:05:57.020 --> 00:05:59.259 So I had to bring that up as a a big one.

NOTE Confidence: 0.884970118

00:05:59.260 --> 00:06:01.703 But Chagas disease is a really big

NOTE Confidence: 0.884970118

00:06:01.703 --> 00:06:03.854 problem in Central and South America

NOTE Confidence: 0.884970118

00:06:03.854 --> 00:06:06.255 as a cause of myocarditis and then

NOTE Confidence: 0.884970118

00:06:06.323 --> 00:06:08.537 we can also rarely see bacterial

NOTE Confidence: 0.884970118

00:06:08.537 --> 00:06:10.397 forms of myocarditis as well.

NOTE Confidence: 0.884970118

00:06:10.397 --> 00:06:13.036 There's also a number of non infectious.

NOTE Confidence: 0.884970118

00:06:13.040 --> 00:06:14.423 Forms of myocarditis,

NOTE Confidence: 0.884970118

00:06:14.423 --> 00:06:16.728 autoimmune diseases such as lupus,

NOTE Confidence: 0.884970118

00:06:16.730 --> 00:06:18.765 treatment related processes such as

NOTE Confidence: 0.884970118

00:06:18.765 --> 00:06:20.800 immune checkpoint and inhibitor myocarditis,

NOTE Confidence: 0.884970118

00:06:20.800 --> 00:06:22.680 something which didn't exist 10

NOTE Confidence: 0.884970118

00:06:22.680 --> 00:06:24.184 or 15 years ago,

NOTE Confidence: 0.884970118

00:06:24.190 --> 00:06:26.350 antipsychotic agents and then

NOTE Confidence: 0.884970118

00:06:26.350 --> 00:06:27.970 even post vaccinations.

NOTE Confidence: 0.884970118

00:06:27.970 --> 00:06:29.965 So there has been some reports which

NOTE Confidence: 0.884970118

00:06:29.965 --> 00:06:32.001 I think percentage of which are real

NOTE Confidence: 0.884970118

00:06:32.001 --> 00:06:34.000 that there are associations with the SARS,

NOTE Confidence: 0.884970118

00:06:34.000 --> 00:06:36.280 Kobe 2 vaccines and some

NOTE Confidence: 0.884970118

00:06:36.280 --> 00:06:38.560 other vaccines that have been

NOTE Confidence: 0.926939567857143

00:06:38.646 --> 00:06:40.418 reported in the past.

NOTE Confidence: 0.926939567857143

00:06:40.420 --> 00:06:42.484 There are also many different subtypes

NOTE Confidence: 0.926939567857143

00:06:42.484 --> 00:06:44.473 of myocarditis and this is again

NOTE Confidence: 0.926939567857143

00:06:44.473 --> 00:06:46.135 from a Histology point of view.

NOTE Confidence: 0.926939567857143

00:06:46.140 --> 00:06:48.744 We have what I call our garden

NOTE Confidence: 0.926939567857143

00:06:48.744 --> 00:06:49.860 variety lymphocytic myocarditis,

NOTE Confidence: 0.926939567857143

00:06:49.860 --> 00:06:52.500 lots of lymphocytes and myocyte damage.

NOTE Confidence: 0.926939567857143

00:06:52.500 --> 00:06:54.840 We have giant cell myocarditis,

NOTE Confidence: 0.926939567857143

00:06:54.840 --> 00:06:57.630 a very specific entity of myocarditis,

NOTE Confidence: 0.926939567857143

00:06:57.630 --> 00:06:59.736 notable by the presence of these

NOTE Confidence: 0.926939567857143

00:06:59.736 --> 00:07:02.680 large giant cells in the mix and a

NOTE Confidence: 0.926939567857143

00:07:02.680 --> 00:07:04.520 very aggressive form of myocarditis.

NOTE Confidence: 0.926939567857143

00:07:04.520 --> 00:07:07.220 And we can even have eosinophilic

NOTE Confidence: 0.926939567857143

00:07:07.220 --> 00:07:09.020 myocarditis with numerous eosinophils

NOTE Confidence: 0.926939567857143

00:07:09.092 --> 00:07:10.868 infiltrating from a variety.

NOTE Confidence: 0.926939567857143

00:07:10.870 --> 00:07:15.178 Processes one other.

NOTE Confidence: 0.926939567857143

00:07:15.180 --> 00:07:16.564 Type that gets lamped,

NOTE Confidence: 0.926939567857143

00:07:16.564 --> 00:07:18.294 lumped in with the other

NOTE Confidence: 0.926939567857143

00:07:18.294 --> 00:07:19.939 myocarditis forms is sarcoidosis,

NOTE Confidence: 0.926939567857143

00:07:19.940 --> 00:07:21.440 which is considered a

NOTE Confidence: 0.926939567857143

00:07:21.440 --> 00:07:22.190 granulomatous myocarditis.

NOTE Confidence: 0.926939567857143

00:07:22.190 --> 00:07:23.618 Some people might distinguish

NOTE Confidence: 0.926939567857143

00:07:23.618 --> 00:07:25.760 sarcoid as being a different process

NOTE Confidence: 0.926939567857143

00:07:25.816 --> 00:07:27.706 because it affects the entire body.

NOTE Confidence: 0.926939567857143

00:07:27.710 --> 00:07:30.559 A lot of people in the myocarditis

NOTE Confidence: 0.926939567857143

00:07:30.559 --> 00:07:34.130 world put it in as part of the process.

NOTE Confidence: 0.926939567857143

00:07:34.130 --> 00:07:36.326 There are a number of clinical

NOTE Confidence: 0.926939567857143

00:07:36.326 --> 00:07:38.289 features of myocarditis that we see,

NOTE Confidence: 0.926939567857143

00:07:38.290 --> 00:07:39.674 a big one being chest pain and I

NOTE Confidence: 0.926939567857143

00:07:39.674 --> 00:07:41.067 stole this picture off the Internet.

NOTE Confidence: 0.926939567857143

00:07:41.070 --> 00:07:43.886 I just thought it was a good example.

NOTE Confidence: 0.926939567857143

00:07:43.890 --> 00:07:46.258 New onset heart failure,

NOTE Confidence: 0.926939567857143

00:07:46.258 --> 00:07:48.626 arrhythmias and conduction disturbances,

NOTE Confidence: 0.926939567857143

00:07:48.630 --> 00:07:49.971 hemodynamic compromise and

NOTE Confidence: 0.926939567857143

00:07:49.971 --> 00:07:51.759 unfortunately debt where there's

NOTE Confidence: 0.926939567857143

00:07:51.759 --> 00:07:54.392 a report of over 40,000 yearly

NOTE Confidence: 0.926939567857143

00:07:54.392 --> 00:07:56.437 deaths from forms of myocarditis.

NOTE Confidence: 0.926939567857143

00:07:56.440 --> 00:07:57.854 A lot of that is Chagas disease,

NOTE Confidence: 0.926939567857143

00:07:57.860 --> 00:08:00.188 sort of chronic processes from that,

NOTE Confidence: 0.926939567857143

00:08:00.190 --> 00:08:00.946 but it also,

NOTE Confidence: 0.926939567857143

00:08:00.946 --> 00:08:02.458 we see this as viral myocarditis

NOTE Confidence: 0.926939567857143

00:08:02.458 --> 00:08:03.817 here in the United States.

NOTE Confidence: 0.926939567857143

00:08:03.820 --> 00:08:05.112 Which unfortunately takes some

NOTE Confidence: 0.926939567857143

00:08:05.112 --> 00:08:06.727 number of lives every year.

NOTE Confidence: 0.858544789444444

00:08:09.160 --> 00:08:11.722 So let's spend a little time talking

NOTE Confidence: 0.858544789444444

00:08:11.722 --> 00:08:13.658 about how myocarditis is diagnosed

NOTE Confidence: 0.858544789444444

00:08:13.658 --> 00:08:15.974 and we have biopsy based approaches,

NOTE Confidence: 0.858544789444444

00:08:15.980 --> 00:08:18.272 imaging based approaches and

NOTE Confidence: 0.858544789444444

00:08:18.272 --> 00:08:21.137 clinically based approaches as well.

NOTE Confidence: 0.858544789444444

00:08:21.140 --> 00:08:22.965 And let's start with the

NOTE Confidence: 0.858544789444444

00:08:22.965 --> 00:08:23.695 endomyocardial biopsy.

NOTE Confidence: 0.858544789444444

00:08:23.700 --> 00:08:25.120 So endomyocardial biopsies are

NOTE Confidence: 0.858544789444444

00:08:25.120 --> 00:08:27.250 performed here with the caves bioptome

NOTE Confidence: 0.858544789444444

00:08:27.305 --> 00:08:28.850 where they take this bioptome,

NOTE Confidence: 0.858544789444444

00:08:28.850 --> 00:08:31.636 they go through the internal jugular vein,

NOTE Confidence: 0.858544789444444

00:08:31.640 --> 00:08:33.768 go into the right side of the heart

NOTE Confidence: 0.858544789444444

00:08:33.768 --> 00:08:35.760 onto the septum and with little

NOTE Confidence: 0.858544789444444

00:08:35.760 --> 00:08:37.510 pinchers they grab little pieces

NOTE Confidence: 0.858544789444444

00:08:37.510 --> 00:08:39.796 of myocardium that look like this.

NOTE Confidence: 0.858544789444444

00:08:39.800 --> 00:08:40.772 They pull it out,

NOTE Confidence: 0.858544789444444

00:08:40.772 --> 00:08:43.510 they give it to us and we make a diagnosis.

NOTE Confidence: 0.858544789444444

00:08:43.510 --> 00:08:45.250 Typically we see from three

NOTE Confidence: 0.858544789444444

00:08:45.250 --> 00:08:46.990 to five pieces of myocardium,

NOTE Confidence: 0.858544789444444

00:08:46.990 --> 00:08:48.445 these small pieces from which

NOTE Confidence: 0.858544789444444

00:08:48.445 --> 00:08:50.510 we're asked to make the diagnosis.

NOTE Confidence: 0.858544789444444

00:08:50.510 --> 00:08:53.009 And then in the setting of myocarditis,

NOTE Confidence: 0.858544789444444

00:08:53.010 --> 00:08:55.250 we're looking for inflammatory cell

NOTE Confidence: 0.858544789444444

00:08:55.250 --> 00:08:57.042 infiltrates and myocyte damage.

NOTE Confidence: 0.858544789444444

00:08:57.050 --> 00:08:59.545 I've highlighted with a CD3A

NOTE Confidence: 0.858544789444444

00:08:59.545 --> 00:09:02.210 number of lymphocytes and with a

NOTE Confidence: 0.858544789444444

00:09:02.210 --> 00:09:04.550 C68A number of macrophages here.

NOTE Confidence: 0.858544789444444

00:09:04.550 --> 00:09:07.544 And we base this diagnosis of

NOTE Confidence: 0.858544789444444

00:09:07.544 --> 00:09:10.450 myocarditis on the Dallas criteria.

NOTE Confidence: 0.858544789444444

00:09:10.450 --> 00:09:12.394 Which I'm going to spend some

NOTE Confidence: 0.858544789444444

00:09:12.394 --> 00:09:14.308 more time talking about in a bit.

NOTE Confidence: 0.858544789444444

00:09:14.310 --> 00:09:17.126 I think this was a very useful paper

NOTE Confidence: 0.858544789444444

00:09:17.126 --> 00:09:19.502 that came out for clinicians which

NOTE Confidence: 0.858544789444444

00:09:19.502 --> 00:09:22.037 was the when to biopsy guidelines

NOTE Confidence: 0.858544789444444

00:09:22.037 --> 00:09:24.470 from 2007 and it has, I don't know,

NOTE Confidence: 0.858544789444444

00:09:24.470 --> 00:09:26.017 I think you can see that OK,

NOTE Confidence: 0.858544789444444

00:09:26.020 --> 00:09:27.310 but I'll I'll talk through it.

NOTE Confidence: 0.858544789444444

00:09:27.310 --> 00:09:29.188 It's a number of different clinical

NOTE Confidence: 0.858544789444444

00:09:29.188 --> 00:09:30.727 scenarios which are either good

NOTE Confidence: 0.858544789444444

00:09:30.727 --> 00:09:32.149 ideas to biopsy or maybe not

NOTE Confidence: 0.858544789444444

00:09:32.149 --> 00:09:33.618 as good ideas to biopsy for.

NOTE Confidence: 0.858544789444444

00:09:33.620 --> 00:09:35.748 And I put green arrows next to the

NOTE Confidence: 0.858544789444444

00:09:35.748 --> 00:09:37.569 scenarios where we're more likely to

NOTE Confidence: 0.858544789444444

00:09:37.569 --> 00:09:39.417 make the diagnosis of myocarditis and

NOTE Confidence: 0.858544789444444

00:09:39.479 --> 00:09:41.396 the ones at the top and the ones here

NOTE Confidence: 0.858544789444444

00:09:41.396 --> 00:09:44.370 as well are new onset heart failure.

NOTE Confidence: 0.858544789444444

00:09:44.370 --> 00:09:46.326 Of either less than two weeks

NOTE Confidence: 0.858544789444444

00:09:46.326 --> 00:09:48.422 duration or two weeks to three

NOTE Confidence: 0.858544789444444

00:09:48.422 --> 00:09:50.242 months duration can be associated

NOTE Confidence: 0.858544789444444

00:09:50.242 --> 00:09:52.359 with a dilated left ventricle,

NOTE Confidence: 0.858544789444444

00:09:52.360 --> 00:09:54.560 new ventricular arrhythmias and then

NOTE Confidence: 0.858544789444444

00:09:54.560 --> 00:09:57.372 here it's basically the same duration

NOTE Confidence: 0.858544789444444

00:09:57.372 --> 00:09:59.536 with some other symptomatology.

NOTE Confidence: 0.858544789444444

00:09:59.540 --> 00:10:02.500 So those scenarios are good times to look

NOTE Confidence: 0.858544789444444

00:10:02.500 --> 00:10:05.385 for myocarditis, new onset myocarditis.

NOTE Confidence: 0.858544789444444

00:10:05.385 --> 00:10:07.530 In a patient.

NOTE Confidence: 0.858544789444444

00:10:07.530 --> 00:10:11.224 No evidence was listed as AB or C&A is

NOTE Confidence: 0.858544789444444

00:10:11.224 --> 00:10:13.846 like your best evidence like randomized

NOTE Confidence: 0.858544789444444

00:10:13.846 --> 00:10:16.729 control trials with placebos and all that.

NOTE Confidence: 0.858544789444444

00:10:16.730 --> 00:10:18.410 There aren't any or at least

NOTE Confidence: 0.858544789444444

00:10:18.410 --> 00:10:19.879 there weren't any of 2007.

NOTE Confidence: 0.858544789444444

00:10:19.879 --> 00:10:21.973 So then B was other trials

NOTE Confidence: 0.858544789444444

00:10:21.973 --> 00:10:24.690 and C was experts best guess.

NOTE Confidence: 0.858544789444444

00:10:24.690 --> 00:10:26.910 And so you can see that even then

NOTE Confidence: 0.858544789444444

00:10:26.910 --> 00:10:29.430 there was a lot of experts best

NOTE Confidence: 0.858544789444444

00:10:29.430 --> 00:10:32.460 guess as to when we're good good

NOTE Confidence: 0.858544789444444

00:10:32.460 --> 00:10:34.240 times to perform biopsies.

NOTE Confidence: 0.858544789444444

00:10:34.240 --> 00:10:36.196 Another approach that people have is

NOTE Confidence: 0.858544789444444

00:10:36.196 --> 00:10:38.878 to do this by imaging cardiac MRI.

NOTE Confidence: 0.858544789444444

00:10:38.880 --> 00:10:40.777 And so they went to Lake Louise,

NOTE Confidence: 0.858544789444444

00:10:40.780 --> 00:10:43.228 which is a beautiful place up in Canada

NOTE Confidence: 0.858544789444444

00:10:43.228 --> 00:10:46.017 and came up with the Lake Louise criteria.

NOTE Confidence: 0.858544789444444

00:10:46.020 --> 00:10:47.000 A few years later,

NOTE Confidence: 0.858544789444444

00:10:47.000 --> 00:10:48.225 needing an excuse to probably

NOTE Confidence: 0.858544789444444

00:10:48.225 --> 00:10:49.338 go back to the lake,

NOTE Confidence: 0.858544789444444

00:10:49.340 --> 00:10:51.830 they came back with revised Lake

NOTE Confidence: 0.858544789444444

00:10:51.830 --> 00:10:53.966 Louise criteria which were improved

NOTE Confidence: 0.858544789444444

00:10:53.966 --> 00:10:56.372 over the original criteria and these

NOTE Confidence: 0.858544789444444

00:10:56.372 --> 00:10:59.340 used T1 and T2 imaging of the heart.

NOTE Confidence: 0.858544789444444

00:10:59.340 --> 00:11:02.130 So on the left we see a T1 weighted

NOTE Confidence: 0.858544789444444

00:11:02.130 --> 00:11:04.590 inversion recovery with Lake gadolinium.

NOTE Confidence: 0.858544789444444

00:11:04.590 --> 00:11:06.350 Enhancement and the orthogonal short

NOTE Confidence: 0.858544789444444

00:11:06.350 --> 00:11:08.717 axis view and what they're seeing I

NOTE Confidence: 0.858544789444444

00:11:08.717 --> 00:11:10.909 believe is this pattern here in the wall

NOTE Confidence: 0.793030344666667

00:11:10.965 --> 00:11:13.114 here this is T2 mapping which highlights

NOTE Confidence: 0.793030344666667

00:11:13.114 --> 00:11:15.452 fluid and it's showing mid wall edema.

NOTE Confidence: 0.793030344666667

00:11:15.452 --> 00:11:17.990 So in this black circle you see

NOTE Confidence: 0.793030344666667

00:11:17.990 --> 00:11:20.066 a little extra fluid that little

NOTE Confidence: 0.793030344666667

00:11:20.066 --> 00:11:22.378 pale area and in that same area

NOTE Confidence: 0.793030344666667

00:11:22.378 --> 00:11:24.690 again on T1 weighted inversion

NOTE Confidence: 0.793030344666667

00:11:24.690 --> 00:11:26.970 recovery Lake gadolinium enhancement

NOTE Confidence: 0.793030344666667

00:11:26.970 --> 00:11:29.838 shows that same area of edema.

NOTE Confidence: 0.793030344666667

00:11:29.840 --> 00:11:33.640 So putting these features together a good.

NOTE Confidence: 0.793030344666667

00:11:33.640 --> 00:11:34.880 I'll just.

NOTE Confidence: 0.888436602941176

00:12:04.460 --> 00:12:06.842 Sometimes I feel that these criteria

NOTE Confidence: 0.888436602941176

00:12:06.842 --> 00:12:09.104 get used in scenarios where they

NOTE Confidence: 0.888436602941176

00:12:09.104 --> 00:12:11.724 may not be as useful a well known.

NOTE Confidence: 0.888436602941176

00:12:11.724 --> 00:12:13.196 Scenario where this occurred

NOTE Confidence: 0.888436602941176

00:12:13.196 --> 00:12:15.559 was in the setting of COVID,

NOTE Confidence: 0.888436602941176

00:12:15.560 --> 00:12:17.456 and so a very influential paper

NOTE Confidence: 0.888436602941176

00:12:17.456 --> 00:12:19.798 came out in the summer of 2020,

NOTE Confidence: 0.888436602941176

00:12:19.800 --> 00:12:21.522 just a few months after COVID

NOTE Confidence: 0.888436602941176

00:12:21.522 --> 00:12:23.080 really became a big thing.

NOTE Confidence: 0.888436602941176

00:12:23.080 --> 00:12:24.720 This came out of Germany,

NOTE Confidence: 0.888436602941176

00:12:24.720 --> 00:12:26.768 and it was a study of 100 patients

NOTE Confidence: 0.888436602941176

00:12:26.768 --> 00:12:29.120 who had just recovered from COVID-19.

NOTE Confidence: 0.888436602941176

00:12:29.120 --> 00:12:31.660 Cardiac MRI revealed that 78%

NOTE Confidence: 0.888436602941176

00:12:31.660 --> 00:12:33.640 of them had cardiac involvement,

NOTE Confidence: 0.888436602941176

00:12:33.640 --> 00:12:36.388 and cardiac MRI suggested that 60%

NOTE Confidence: 0.888436602941176

00:12:36.388 --> 00:12:39.140 had ongoing myocardial inflammation.

NOTE Confidence: 0.888436602941176

00:12:39.140 --> 00:12:42.255 So 60% of people who had COVID,

NOTE Confidence: 0.888436602941176

00:12:42.260 --> 00:12:45.926 they claim now. Had. No.

NOTE Confidence: 0.888436602941176

00:12:45.926 --> 00:12:49.740 Per diem. I to a lot of us,

NOTE Confidence: 0.888436602941176

00:12:49.740 --> 00:12:51.636 I remember calling my cardiology colleagues,

NOTE Confidence: 0.888436602941176

00:12:51.640 --> 00:12:53.530 I said, are you seeing 6 of 10 patients

NOTE Confidence: 0.888436602941176

00:12:53.530 --> 00:12:55.208 who had COVID having myocarditis?

NOTE Confidence: 0.888436602941176

00:12:55.210 --> 00:12:56.380 And they said, no, we're not,

NOTE Confidence: 0.888436602941176

00:12:56.380 --> 00:12:58.240 we're not seeing this at all.

NOTE Confidence: 0.888436602941176

00:12:58.240 --> 00:13:00.158 I, I and others became very upset.

NOTE Confidence: 0.888436602941176

00:13:00.160 --> 00:13:01.700 I reached out to circulation and said

NOTE Confidence: 0.888436602941176

00:13:01.700 --> 00:13:03.677 we got to write something about this.

NOTE Confidence: 0.888436602941176

00:13:03.680 --> 00:13:05.556 And I got a note back saying,

NOTE Confidence: 0.888436602941176

00:13:05.560 --> 00:13:06.740 yeah, you can write something,

NOTE Confidence: 0.888436602941176

00:13:06.740 --> 00:13:08.658 but you can't do a hit piece

NOTE Confidence: 0.888436602941176

00:13:08.658 --> 00:13:10.380 or takedown of that article.

NOTE Confidence: 0.888436602941176

00:13:10.380 --> 00:13:12.388 So we, we kind of talked around it,

NOTE Confidence: 0.888436602941176

00:13:12.390 --> 00:13:14.340 but other people went after

NOTE Confidence: 0.888436602941176

00:13:14.340 --> 00:13:15.120 this specifically.

NOTE Confidence: 0.888436602941176

00:13:15.120 --> 00:13:16.638 And one of the problems was

NOTE Confidence: 0.888436602941176

00:13:16.638 --> 00:13:17.920 when this paper came out.

NOTE Confidence: 0.888436602941176

00:13:17.920 --> 00:13:19.620 In the middle of 2020,

NOTE Confidence: 0.888436602941176

00:13:19.620 --> 00:13:21.268 we didn't have a lot of data to

NOTE Confidence: 0.888436602941176

00:13:21.268 --> 00:13:22.668 prove that they weren't right,

NOTE Confidence: 0.888436602941176

00:13:22.670 --> 00:13:24.350 and again, it just seemed,

NOTE Confidence: 0.888436602941176

00:13:24.350 --> 00:13:27.848 anecdotally, really excessive.

NOTE Confidence: 0.888436602941176

00:13:27.850 --> 00:13:29.938 So I was able to work with Rick

NOTE Confidence: 0.888436602941176

00:13:29.938 --> 00:13:31.944 Vanderheide who was at LSU at the time

NOTE Confidence: 0.888436602941176

00:13:31.944 --> 00:13:34.067 and we collected all of the autopsy data.

NOTE Confidence: 0.888436602941176

00:13:34.070 --> 00:13:36.440 We could get all the autopsy

NOTE Confidence: 0.888436602941176

00:13:36.440 --> 00:13:38.709 series that were coming out with

NOTE Confidence: 0.888436602941176

00:13:38.710 --> 00:13:40.714 102030 cases from around the world

NOTE Confidence: 0.888436602941176

00:13:40.714 --> 00:13:42.552 and say what's the incidence

NOTE Confidence: 0.888436602941176

00:13:42.552 --> 00:13:44.707 of myocarditis and these cases.

NOTE Confidence: 0.888436602941176

00:13:44.710 --> 00:13:46.310 So these are people who died of COVID,

NOTE Confidence: 0.888436602941176

00:13:46.310 --> 00:13:47.741 so severe COVID,

NOTE Confidence: 0.888436602941176

00:13:47.741 --> 00:13:50.603 how much myocarditis are we seeing?

NOTE Confidence: 0.888436602941176

00:13:50.610 --> 00:13:52.930 And the answer was that we felt the

NOTE Confidence: 0.888436602941176

00:13:52.930 --> 00:13:54.936 true prevalence of myocarditis based on

NOTE Confidence: 0.888436602941176

00:13:54.936 --> 00:13:56.982 these autopsy series was much lower,

NOTE Confidence: 0.888436602941176

00:13:56.990 --> 00:13:57.700 probably less.

NOTE Confidence: 0.888436602941176

00:13:57.700 --> 00:13:58.410 And 2%,

NOTE Confidence: 0.888436602941176

00:13:58.410 --> 00:14:00.944 which seems to be more reasonable relative

NOTE Confidence: 0.888436602941176

00:14:00.944 --> 00:14:03.592 to data that has come since that time.

NOTE Confidence: 0.888436602941176

00:14:03.600 --> 00:14:05.049 Now we noticed a couple other things

NOTE Confidence: 0.888436602941176

00:14:05.049 --> 00:14:06.520 when we were doing this project.

NOTE Confidence: 0.888436602941176

00:14:06.520 --> 00:14:08.774 One is that people were using those

NOTE Confidence: 0.888436602941176

00:14:08.774 --> 00:14:10.900 Dallas criteria that I mentioned before,

NOTE Confidence: 0.888436602941176

00:14:10.900 --> 00:14:13.130 something we use for endomyocardial

NOTE Confidence: 0.888436602941176

00:14:13.130 --> 00:14:16.586 biopsy to make the diagnosis on X or

NOTE Confidence: 0.888436602941176

00:14:16.586 --> 00:14:18.500 deceased people's hearts, autopsy hearts.

NOTE Confidence: 0.888436602941176

00:14:18.500 --> 00:14:20.780 And it's not designed for that.

NOTE Confidence: 0.888436602941176

00:14:20.780 --> 00:14:22.680 It's designed specifically for biopsy.

NOTE Confidence: 0.888436602941176

00:14:22.680 --> 00:14:24.872 So that was inappropriate.

NOTE Confidence: 0.888436602941176

00:14:24.872 --> 00:14:25.420 Secondly,

NOTE Confidence: 0.888436602941176

00:14:25.420 --> 00:14:26.480 in a lot of series,

NOTE Confidence: 0.888436602941176

00:14:26.480 --> 00:14:29.978 people were suggesting they had seen.

NOTE Confidence: 0.888436602941176

00:14:29.980 --> 00:14:32.176 Myocarditis and showed a picture of

NOTE Confidence: 0.888436602941176

00:14:32.176 --> 00:14:34.460 what they described as myocarditis.

NOTE Confidence: 0.888436602941176

00:14:34.460 --> 00:14:35.832 But you look at that picture and

NOTE Confidence: 0.888436602941176

00:14:35.832 --> 00:14:36.982 say that's really not myocarditis

NOTE Confidence: 0.888436602941176

00:14:36.982 --> 00:14:37.759 and there's some,

NOTE Confidence: 0.888436602941176

00:14:37.760 --> 00:14:39.816 maybe a few more immune cells than expected,

NOTE Confidence: 0.888436602941176

00:14:39.820 --> 00:14:41.836 but we're not seeing the right

NOTE Confidence: 0.888436602941176

00:14:41.836 --> 00:14:42.844 features for myocarditis.

NOTE Confidence: 0.888436602941176

00:14:42.850 --> 00:14:44.460 And if you're showing me a picture,

NOTE Confidence: 0.888436602941176

00:14:44.460 --> 00:14:46.371 I would think you'd be taking the

NOTE Confidence: 0.888436602941176

00:14:46.371 --> 00:14:48.270 most obvious part of the myocarditis.

NOTE Confidence: 0.888436602941176

00:14:48.270 --> 00:14:49.936 So it LED us to believe that

NOTE Confidence: 0.888436602941176

00:14:49.936 --> 00:14:51.240 even in this scenario,

NOTE Confidence: 0.888436602941176

00:14:51.240 --> 00:14:52.580 some people were misusing

NOTE Confidence: 0.888436602941176

00:14:52.580 --> 00:14:54.590 the tools that we have to

NOTE Confidence: 0.888030066666667

00:14:54.662 --> 00:14:56.897 make the diagnosis of myocarditis.

NOTE Confidence: 0.888030066666667

00:14:56.900 --> 00:15:00.250 So that is a challenge.

NOTE Confidence: 0.888030066666667

00:15:00.250 --> 00:15:02.254 Some people have to make the

NOTE Confidence: 0.888030066666667

00:15:02.254 --> 00:15:03.590 diagnosis of myocarditis purely

NOTE Confidence: 0.888030066666667

00:15:03.647 --> 00:15:05.147 based on clinical features.

NOTE Confidence: 0.888030066666667

00:15:05.150 --> 00:15:07.250 No access to cardiac MRI,

NOTE Confidence: 0.888030066666667

00:15:07.250 --> 00:15:10.370 no access to endomyocardial biopsy.

NOTE Confidence: 0.888030066666667

00:15:10.370 --> 00:15:11.690 And these features include chest

NOTE Confidence: 0.888030066666667

00:15:11.690 --> 00:15:13.430 pain like I talked about earlier,

NOTE Confidence: 0.888030066666667

00:15:13.430 --> 00:15:16.550 St segment elevation on an EKG,

NOTE Confidence: 0.888030066666667

00:15:16.550 --> 00:15:18.182 elevations of erythrocyte

NOTE Confidence: 0.888030066666667

00:15:18.182 --> 00:15:20.358 sedimentation rate or CRP,

NOTE Confidence: 0.888030066666667

00:15:20.360 --> 00:15:22.832 high sensitivity troponin or

NOTE Confidence: 0.888030066666667

00:15:22.832 --> 00:15:26.540 elevated CKMB NT Pro BNP elevations

NOTE Confidence: 0.888030066666667

00:15:26.641 --> 00:15:29.248 and cardiac autoantibodies.

NOTE Confidence: 0.888030066666667

00:15:29.250 --> 00:15:29.784 However,

NOTE Confidence: 0.888030066666667

00:15:29.784 --> 00:15:32.988 all of these are nonspecific findings.

NOTE Confidence: 0.888030066666667

00:15:32.990 --> 00:15:35.915 So you can see all of these in other

NOTE Confidence: 0.888030066666667

00:15:35.915 --> 00:15:37.390 cardiovascular related diseases.

NOTE Confidence: 0.888030066666667

00:15:37.390 --> 00:15:39.460 Chest pain you obviously can

NOTE Confidence: 0.888030066666667

00:15:39.460 --> 00:15:41.116 see a myocardial infarction.

NOTE Confidence: 0.888030066666667

00:15:41.120 --> 00:15:43.100 Have that in aortic dissection.

NOTE Confidence: 0.888030066666667

00:15:43.100 --> 00:15:44.220 People even complain of

NOTE Confidence: 0.888030066666667

00:15:44.220 --> 00:15:45.620 chest pain who have GERD,

NOTE Confidence: 0.888030066666667

00:15:45.620 --> 00:15:47.840 so not the most specific thing.

NOTE Confidence: 0.888030066666667

00:15:47.840 --> 00:15:50.206 And all the other features can be

NOTE Confidence: 0.888030066666667

00:15:50.206 --> 00:15:52.429 seen in other either myocardial

NOTE Confidence: 0.888030066666667

00:15:52.429 --> 00:15:54.685 infarctions or heart failure.

NOTE Confidence: 0.888030066666667

00:15:54.690 --> 00:15:56.650 So we all got excited last year

NOTE Confidence: 0.888030066666667

00:15:56.650 --> 00:15:58.645 when a paper came out describing

NOTE Confidence: 0.888030066666667

00:15:58.645 --> 00:16:00.823 a new blood based biomarker which

NOTE Confidence: 0.888030066666667

00:16:00.823 --> 00:16:03.816 was initially called HSA Mirror

NOTE Confidence: 0.888030066666667

00:16:03.816 --> 00:16:05.870 chromosome 896 and I want to

NOTE Confidence: 0.888030066666667

00:16:05.870 --> 00:16:07.490 spend a moment talking about this.

NOTE Confidence: 0.888030066666667

00:16:07.490 --> 00:16:09.682 So this came out in the New England

NOTE Confidence: 0.888030066666667

00:16:09.682 --> 00:16:12.890 Journal of Medicine in May of 2021.

NOTE Confidence: 0.888030066666667

00:16:12.890 --> 00:16:13.259 And it was.

NOTE Confidence: 0.764091064166667

00:16:16.250 --> 00:16:18.260 Called the novel circulating micro RNA

NOTE Confidence: 0.764091064166667

00:16:18.260 --> 00:16:20.689 for the detection of acute myocarditis.

NOTE Confidence: 0.764091064166667

00:16:20.690 --> 00:16:21.698 Within just a couple of days

NOTE Confidence: 0.764091064166667

00:16:21.698 --> 00:16:22.550 of this paper coming out,

NOTE Confidence: 0.764091064166667

00:16:22.550 --> 00:16:23.760 I've gotten multiple emails from

NOTE Confidence: 0.764091064166667

00:16:23.760 --> 00:16:25.250 colleagues from all over the place.

NOTE Confidence: 0.764091064166667

00:16:25.250 --> 00:16:27.105 Hey, Mark, have you seen this paper?

NOTE Confidence: 0.764091064166667

00:16:27.110 --> 00:16:28.629 And the reason they asked is because,

NOTE Confidence: 0.764091064166667

00:16:28.630 --> 00:16:30.034 well, I'm a cardiovascular

NOTE Confidence: 0.764091064166667

00:16:30.034 --> 00:16:32.075 pathologist and I do micro RNA's.

NOTE Confidence: 0.764091064166667

00:16:32.075 --> 00:16:34.070 And so that's clearly in my wheelhouse

NOTE Confidence: 0.764091064166667

00:16:34.070 --> 00:16:36.248 of things that I would be interested in.

NOTE Confidence: 0.764091064166667

00:16:36.250 --> 00:16:37.438 And I was like, yeah, thank you.

NOTE Confidence: 0.764091064166667

00:16:37.438 --> 00:16:40.570 I did see it and I'm reading it right now.

NOTE Confidence: 0.764091064166667

00:16:40.570 --> 00:16:42.874 And So what they did was they started

NOTE Confidence: 0.764091064166667

00:16:42.874 --> 00:16:44.925 with a mouse and it's known that

NOTE Confidence: 0.764091064166667

00:16:44.925 --> 00:16:47.583 TH 17 cells and a type of immune

NOTE Confidence: 0.764091064166667

00:16:47.583 --> 00:16:49.548 cell is increased in myocarditis.

NOTE Confidence: 0.764091064166667

00:16:49.550 --> 00:16:52.784 And they found a micro RNA called

NOTE Confidence: 0.764091064166667

00:16:52.784 --> 00:16:55.865 mere 721 and micronas are just

NOTE Confidence: 0.764091064166667

00:16:55.865 --> 00:16:58.988 numbered short RNA's 21 bases or so.

NOTE Confidence: 0.764091064166667

00:16:58.990 --> 00:17:00.446 And I could go into much more detail,

NOTE Confidence: 0.764091064166667

00:17:00.450 --> 00:17:02.130 but I'll try and keep it simple.

NOTE Confidence: 0.764091064166667

00:17:02.130 --> 00:17:04.874 They found that this mere 721 in

NOTE Confidence: 0.764091064166667

00:17:04.874 --> 00:17:07.346 mice was elevated in myocarditis as

NOTE Confidence: 0.764091064166667

00:17:07.346 --> 00:17:10.679 seen here and it was not elevated

NOTE Confidence: 0.764091064166667

00:17:10.679 --> 00:17:12.134 in mycardial infarctions.

NOTE Confidence: 0.764091064166667

00:17:12.140 --> 00:17:13.236 That was pretty exciting.

NOTE Confidence: 0.764091064166667

00:17:13.236 --> 00:17:14.455 They then said, well,

NOTE Confidence: 0.764091064166667

00:17:14.455 --> 00:17:17.615 what's the human correlate of that micro RNA?

NOTE Confidence: 0.764091064166667

00:17:17.620 --> 00:17:19.318 And they found a sequence on

NOTE Confidence: 0.764091064166667

00:17:19.318 --> 00:17:21.219 chromosome 8 which they felt matched.

NOTE Confidence: 0.764091064166667

00:17:21.220 --> 00:17:24.208 And then they showed across multiple

NOTE Confidence: 0.764091064166667

00:17:24.208 --> 00:17:27.784 other cohorts that this micro RNA in

NOTE Confidence: 0.764091064166667

00:17:27.784 --> 00:17:30.274 humans was elevated in myocarditis.

NOTE Confidence: 0.764091064166667

00:17:30.280 --> 00:17:33.104 You can see that even normals had some

NOTE Confidence: 0.764091064166667

00:17:33.104 --> 00:17:35.656 expression of this mere chromosome 896,

NOTE Confidence: 0.764091064166667

00:17:35.656 --> 00:17:38.568 but again, it was elevated in myocarditis.

NOTE Confidence: 0.764091064166667

00:17:38.570 --> 00:17:40.360 So this paper came out.

NOTE Confidence: 0.764091064166667

00:17:40.360 --> 00:17:41.820 I think I got excited.

NOTE Confidence: 0.764091064166667

00:17:41.820 --> 00:17:42.771 I had already.

NOTE Confidence: 0.764091064166667

00:17:42.771 --> 00:17:44.673 Published a paper saying use of

NOTE Confidence: 0.764091064166667

00:17:44.673 --> 00:17:46.136 micrornas as cardiovascular biomarkers

NOTE Confidence: 0.764091064166667

00:17:46.136 --> 00:17:48.670 and we specifically said this is an

NOTE Confidence: 0.764091064166667

00:17:48.733 --> 00:17:50.910 area where they might be useful where

NOTE Confidence: 0.764091064166667

00:17:50.910 --> 00:17:52.705 some other places they wouldn't be.

NOTE Confidence: 0.764091064166667

00:17:52.705 --> 00:17:54.700 And at the time I was studying

NOTE Confidence: 0.764091064166667

00:17:54.766 --> 00:17:56.668 micro RNA expression in the lab,

NOTE Confidence: 0.764091064166667

00:17:56.670 --> 00:17:59.538 we had huge datasets of cellular

NOTE Confidence: 0.764091064166667

00:17:59.538 --> 00:18:01.450 microrna expression from sequencing.

NOTE Confidence: 0.764091064166667

00:18:01.450 --> 00:18:04.483 And I reached out to my postdoc a room

NOTE Confidence: 0.764091064166667

00:18:04.483 --> 00:18:06.946 and I said Arun, let's find this sequence,

NOTE Confidence: 0.764091064166667

00:18:06.946 --> 00:18:08.566 let's see where it's expressed.

NOTE Confidence: 0.764091064166667

00:18:08.570 --> 00:18:10.826 Just TH 17 cells or is it found

NOTE Confidence: 0.764091064166667

00:18:10.826 --> 00:18:12.668 in other cells like let's?

NOTE Confidence: 0.764091064166667

00:18:12.670 --> 00:18:13.492 Let's solve this.

NOTE Confidence: 0.764091064166667

00:18:13.492 --> 00:18:15.136 So I sent them scurrying away.

NOTE Confidence: 0.764091064166667

00:18:15.140 --> 00:18:16.736 He comes back a little later

NOTE Confidence: 0.764091064166667

00:18:16.736 --> 00:18:18.150 that day and says Mark.

NOTE Confidence: 0.764091064166667

00:18:18.150 --> 00:18:19.074 I don't see it.

NOTE Confidence: 0.764091064166667

00:18:19.074 --> 00:18:21.250 I can't find it in any of our data.

NOTE Confidence: 0.764091064166667

00:18:21.250 --> 00:18:23.636 I said whoa, whoa, whoa, this is weird.

NOTE Confidence: 0.764091064166667

00:18:23.636 --> 00:18:25.710 Let me go look further at this paper.

NOTE Confidence: 0.764091064166667

00:18:25.710 --> 00:18:28.368 So it turned out there's some

NOTE Confidence: 0.764091064166667

00:18:28.368 --> 00:18:30.730 real problems with this paper,

NOTE Confidence: 0.764091064166667

00:18:30.730 --> 00:18:32.638 which essentially is that

NOTE Confidence: 0.764091064166667

00:18:32.638 --> 00:18:34.546 this sequence doesn't exist.

NOTE Confidence: 0.764091064166667

00:18:34.550 --> 00:18:36.290 There was no micro RNA.

NOTE Confidence: 0.764091064166667

00:18:36.290 --> 00:18:39.890 There's no HSA chromosome 896.

NOTE Confidence: 0.764091064166667

00:18:39.890 --> 00:18:41.750 A couple things to point out

NOTE Confidence: 0.764091064166667

00:18:41.750 --> 00:18:42.990 here on the left.

NOTE Confidence: 0.764091064166667

00:18:42.990 --> 00:18:45.768 This is a normal micro RNA

NOTE Confidence: 0.764091064166667

00:18:45.768 --> 00:18:48.190 structure that you see this.

NOTE Confidence: 0.764091064166667

00:18:48.190 --> 00:18:49.828 It has a hairpin loop of

NOTE Confidence: 0.764091064166667

00:18:49.828 --> 00:18:50.647 roughly this dimension.

NOTE Confidence: 0.764091064166667

00:18:50.650 --> 00:18:54.048 This is the classic HSA Mirror 1/26

NOTE Confidence: 0.764091064166667

00:18:54.048 --> 00:18:57.028 and abundant well described micro RNA

NOTE Confidence: 0.764091064166667

00:18:57.028 --> 00:18:59.220 which they described in the paper as well.

NOTE Confidence: 0.764091064166667

00:18:59.220 --> 00:19:03.015 This is the mouse mirror 721 and this

NOTE Confidence: 0.764091064166667

00:19:03.015 --> 00:19:05.497 is human chromosome chromosome 896,

NOTE Confidence: 0.764091064166667

00:19:05.497 --> 00:19:07.519 which should make a hairpin loop

NOTE Confidence: 0.764091064166667

00:19:07.519 --> 00:19:09.679 but has this crazy structure.

NOTE Confidence: 0.764091064166667

00:19:09.680 --> 00:19:11.521 So that's not going to be part

NOTE Confidence: 0.764091064166667

00:19:11.521 --> 00:19:12.310 of the micro

NOTE Confidence: 0.893566082666667

00:19:12.379 --> 00:19:14.219 RNA machinery to process this.

NOTE Confidence: 0.893566082666667

00:19:14.220 --> 00:19:16.019 That was one thing that was weird.

NOTE Confidence: 0.893566082666667

00:19:16.020 --> 00:19:19.230 The second is that mirror.

NOTE Confidence: 0.893566082666667

00:19:19.230 --> 00:19:21.550 721 is located in the mouse in the

NOTE Confidence: 0.893566082666667

00:19:21.550 --> 00:19:23.688 locus of a gene called Cux one.

NOTE Confidence: 0.893566082666667

00:19:23.690 --> 00:19:25.783 Usually when a micro RNA is in

NOTE Confidence: 0.893566082666667

00:19:25.783 --> 00:19:28.070 a gene and intragenic region,

NOTE Confidence: 0.893566082666667

00:19:28.070 --> 00:19:30.098 it stays in that same regions,

NOTE Confidence: 0.893566082666667

00:19:30.100 --> 00:19:32.938 particularly over a short time period

NOTE Confidence: 0.893566082666667

00:19:32.938 --> 00:19:36.336 such as between mice and human and the

NOTE Confidence: 0.893566082666667

00:19:36.336 --> 00:19:38.394 sequence that they identified was on

NOTE Confidence: 0.893566082666667

00:19:38.394 --> 00:19:40.354 chromosome 8 and may of corresponded

NOTE Confidence: 0.893566082666667

00:19:40.354 --> 00:19:42.709 with a long non coding RNA in mice.

NOTE Confidence: 0.893566082666667

00:19:42.710 --> 00:19:45.230 It was definitely found in the

NOTE Confidence: 0.893566082666667

00:19:45.230 --> 00:19:48.039 area of a long coding RNA.

NOTE Confidence: 0.893566082666667

00:19:48.040 --> 00:19:51.480 Inhuman additionally, and most critically,

NOTE Confidence: 0.893566082666667

00:19:51.480 --> 00:19:53.223 is a micro RNA has an area

NOTE Confidence: 0.893566082666667

00:19:53.223 --> 00:19:54.600 called a seed sequence,

NOTE Confidence: 0.893566082666667

00:19:54.600 --> 00:19:57.832 and this six base or seven base nucleotide

NOTE Confidence: 0.893566082666667

00:19:57.832 --> 00:20:01.117 sequence at the end is completely invariant.

NOTE Confidence: 0.893566082666667

00:20:01.120 --> 00:20:03.608 It's the critical piece for binding of that

NOTE Confidence: 0.893566082666667

00:20:03.608 --> 00:20:06.236 micro RNA to its targets on Messenger RNAs,

NOTE Confidence: 0.893566082666667

00:20:06.240 --> 00:20:08.683 and they propose that two of the

NOTE Confidence: 0.893566082666667

00:20:08.683 --> 00:20:10.340 six nucleotides had changed.

NOTE Confidence: 0.893566082666667

00:20:10.340 --> 00:20:12.321 And the analogy that I have for

NOTE Confidence: 0.893566082666667

00:20:12.321 --> 00:20:13.989 that is suddenly being able to

NOTE Confidence: 0.893566082666667

00:20:13.989 --> 00:20:15.760 use your car key to open your

NOTE Confidence: 0.893566082666667

00:20:15.825 --> 00:20:17.829 house through the key rather than.

NOTE Confidence: 0.893566082666667

00:20:17.830 --> 00:20:19.474 Of your house key.

NOTE Confidence: 0.893566082666667

00:20:19.474 --> 00:20:22.407 It's a massive change in identification and

NOTE Confidence: 0.893566082666667

00:20:22.407 --> 00:20:25.137 everything would have to move in tandem.

NOTE Confidence: 0.893566082666667

00:20:25.140 --> 00:20:26.946 You'd have to switch out all the

NOTE Confidence: 0.893566082666667

00:20:26.946 --> 00:20:28.789 locks in your house at the same

NOTE Confidence: 0.893566082666667

00:20:28.789 --> 00:20:30.301 time to match your car key,

NOTE Confidence: 0.893566082666667

00:20:30.310 --> 00:20:32.230 and we don't have any evidence of that.

NOTE Confidence: 0.893566082666667

00:20:32.230 --> 00:20:34.519 So there's a lot of concerns in

NOTE Confidence: 0.893566082666667

00:20:34.519 --> 00:20:36.829 addition to not finding any reads.

NOTE Confidence: 0.893566082666667

00:20:36.830 --> 00:20:38.510 And when we reached out to a colleague

NOTE Confidence: 0.893566082666667

00:20:38.510 --> 00:20:40.207 who had even more data than we had,

NOTE Confidence: 0.893566082666667

00:20:40.210 --> 00:20:43.360 it wasn't present in 230 billion reads.

NOTE Confidence: 0.893566082666667

00:20:43.360 --> 00:20:44.770 I then additionally I called the

NOTE Confidence: 0.893566082666667

00:20:44.770 --> 00:20:46.120 holistica X Prize on Twitter.

NOTE Confidence: 0.893566082666667

00:20:46.120 --> 00:20:47.488 I said if anyone can find the sequence

NOTE Confidence: 0.893566082666667

00:20:47.488 --> 00:20:49.384 let me know, I'll pay you money.

NOTE Confidence: 0.893566082666667

00:20:49.384 --> 00:20:52.198 And I had a student from somewhere up

NOTE Confidence: 0.893566082666667

00:20:52.198 --> 00:20:55.256 in this area who found 200 base pair

NOTE Confidence: 0.893566082666667

00:20:55.256 --> 00:20:57.216 sequence reads and thyroid tissue,

NOTE Confidence: 0.893566082666667

00:20:57.220 --> 00:20:59.266 again suggesting either this was DNA

NOTE Confidence: 0.893566082666667

00:20:59.266 --> 00:21:01.298 contamination in the RNA sequencing data

NOTE Confidence: 0.893566082666667

00:21:01.298 --> 00:21:03.714 set or it's part of a larger sequence,

NOTE Confidence: 0.893566082666667

00:21:03.720 --> 00:21:06.060 but again not a short RNA.

NOTE Confidence: 0.893566082666667

00:21:06.060 --> 00:21:07.593 And the reason I'm going on and

NOTE Confidence: 0.893566082666667

00:21:07.593 --> 00:21:09.422 on and on about this is because

NOTE Confidence: 0.893566082666667

00:21:09.422 --> 00:21:10.817 we put all this together.

NOTE Confidence: 0.893566082666667

00:21:10.820 --> 00:21:12.040 We let the Newland Journal

NOTE Confidence: 0.893566082666667

00:21:12.040 --> 00:21:13.260 of Medicine know 8 days.

NOTE Confidence: 0.893566082666667

00:21:13.260 --> 00:21:15.990 After the paper came out that they

NOTE Confidence: 0.893566082666667

00:21:15.990 --> 00:21:18.119 were very serious concerns about

NOTE Confidence: 0.893566082666667

00:21:18.119 --> 00:21:20.771 this thing which was proposed as

NOTE Confidence: 0.893566082666667

00:21:20.771 --> 00:21:23.307 a biomarker and Long story short,

NOTE Confidence: 0.893566082666667

00:21:23.310 --> 00:21:25.865 it wasn't put out there to the

NOTE Confidence: 0.893566082666667

00:21:25.865 --> 00:21:27.928 public until September of this year.

NOTE Confidence: 0.893566082666667

00:21:27.930 --> 00:21:30.990 It was of to me embarrassing,

NOTE Confidence: 0.893566082666667

00:21:30.990 --> 00:21:33.288 but they refused to move on.

NOTE Confidence: 0.893566082666667

00:21:33.290 --> 00:21:35.468 This major concern and our major

NOTE Confidence: 0.893566082666667

00:21:35.468 --> 00:21:37.734 concern was please don't let anybody

NOTE Confidence: 0.893566082666667

00:21:37.734 --> 00:21:39.609 study this micro RNA biomarker

NOTE Confidence: 0.893566082666667

00:21:39.609 --> 00:21:41.568 because it's not a micro RNA,

NOTE Confidence: 0.893566082666667

00:21:41.570 --> 00:21:44.167 it's possible and I'm not a purist.

NOTE Confidence: 0.893566082666667

00:21:44.170 --> 00:21:46.648 That any small RNA sequence that can

NOTE Confidence: 0.893566082666667

00:21:46.648 --> 00:21:49.670 serve as a biomarker is a biomarker.

NOTE Confidence: 0.893566082666667

00:21:49.670 --> 00:21:52.685 If we're in green shoes is a good biomarker.

NOTE Confidence: 0.893566082666667

00:21:52.690 --> 00:21:54.670 Then let's look at people's shoes.

NOTE Confidence: 0.893566082666667

00:21:54.670 --> 00:21:55.686 I'm fine with that.

NOTE Confidence: 0.893566082666667

00:21:55.686 --> 00:21:57.630 But there was no connection between the two.

NOTE Confidence: 0.893566082666667

00:21:57.630 --> 00:22:00.158 So they had about a A1 and 2.5

NOTE Confidence: 0.893566082666667

00:22:00.158 --> 00:22:00.790 billion chance,

NOTE Confidence: 0.893566082666667

00:22:00.790 --> 00:22:02.506 assuming the number of RNA that

NOTE Confidence: 0.893566082666667

00:22:02.506 --> 00:22:03.650 you'd see that they

NOTE Confidence: 0.777480535833333

00:22:03.712 --> 00:22:06.738 were right. So a big concern,

NOTE Confidence: 0.777480535833333

00:22:06.738 --> 00:22:09.624 I met with Carlos last night

NOTE Confidence: 0.777480535833333

00:22:09.624 --> 00:22:11.046 and he also agreed with me.

NOTE Confidence: 0.777480535833333

00:22:11.050 --> 00:22:14.614 So I felt very vindicated about all of that.

NOTE Confidence: 0.777480535833333

00:22:14.620 --> 00:22:16.474 OK. So I want to move on and say

NOTE Confidence: 0.777480535833333

00:22:16.474 --> 00:22:18.211 basically that we got excited about a

NOTE Confidence: 0.777480535833333

00:22:18.211 --> 00:22:20.078 biomarker and we don't have a biomarker.

NOTE Confidence: 0.777480535833333

00:22:20.080 --> 00:22:22.810 So let's turn our attention

NOTE Confidence: 0.777480535833333

00:22:22.810 --> 00:22:25.540 back to the Dallas criteria.

NOTE Confidence: 0.777480535833333

00:22:25.540 --> 00:22:29.791 The Dallas criteria came about circa 1985.

NOTE Confidence: 0.777480535833333

00:22:29.791 --> 00:22:32.050 And the reason for this was at that time

NOTE Confidence: 0.777480535833333

00:22:32.104 --> 00:22:34.127 they were trying to do clinical trials

NOTE Confidence: 0.777480535833333

00:22:34.127 --> 00:22:36.214 of steroids to see if immunosuppression

NOTE Confidence: 0.777480535833333

00:22:36.214 --> 00:22:38.154 would be useful for myocarditis.

NOTE Confidence: 0.777480535833333

00:22:38.160 --> 00:22:40.200 And the problem was that pathologists

NOTE Confidence: 0.777480535833333

00:22:40.200 --> 00:22:42.131 didn't have the same criteria

NOTE Confidence: 0.777480535833333

00:22:42.131 --> 00:22:43.670 at different institutions.

NOTE Confidence: 0.777480535833333

00:22:43.670 --> 00:22:45.506 People had different things going on,

NOTE Confidence: 0.777480535833333

00:22:45.510 --> 00:22:46.795 and so they brought everybody

NOTE Confidence: 0.777480535833333

00:22:46.795 --> 00:22:47.566 together in Dallas.

NOTE Confidence: 0.777480535833333

00:22:47.570 --> 00:22:50.090 They got a bunch of microscopes.

NOTE Confidence: 0.777480535833333

00:22:50.090 --> 00:22:52.288 And lots of glass slides of myocarditis

NOTE Confidence: 0.777480535833333

00:22:52.288 --> 00:22:55.133 and they sat down and hammered out some

NOTE Confidence: 0.777480535833333

00:22:55.133 --> 00:22:57.471 criteria which were published here in 1986.

NOTE Confidence: 0.777480535833333

00:22:57.471 --> 00:22:59.648 And they basically had these three levels.

NOTE Confidence: 0.777480535833333

00:22:59.650 --> 00:23:02.710 They had the definition of myocarditis,

NOTE Confidence: 0.777480535833333

00:23:02.710 --> 00:23:04.230 which is myocardial necrosis

NOTE Confidence: 0.777480535833333

00:23:04.230 --> 00:23:06.510 degeneration or both in the absence

NOTE Confidence: 0.777480535833333

00:23:06.579 --> 00:23:08.507 of significant coronary artery

NOTE Confidence: 0.777480535833333

00:23:08.507 --> 00:23:10.435 disease with adjacent inflammatory

NOTE Confidence: 0.777480535833333

00:23:10.435 --> 00:23:12.648 infiltrate with or without fibrosis,

NOTE Confidence: 0.777480535833333

00:23:12.650 --> 00:23:13.548 borderline myocarditis,

NOTE Confidence: 0.777480535833333

00:23:13.548 --> 00:23:15.793 which was this intermediate think

NOTE Confidence: 0.777480535833333

00:23:15.793 --> 00:23:17.950 of dysplasia as a correlate.

NOTE Confidence: 0.777480535833333

00:23:17.950 --> 00:23:19.938 So it's not normal, but it's not.

NOTE Confidence: 0.777480535833333

00:23:19.940 --> 00:23:20.344 Myocarditis,

NOTE Confidence: 0.777480535833333

00:23:20.344 --> 00:23:22.768 so we'll just call it borderline

NOTE Confidence: 0.777480535833333

00:23:22.768 --> 00:23:24.810 myocarditis and no myocarditis,

NOTE Confidence: 0.777480535833333

00:23:24.810 --> 00:23:27.245 no evidence of inflammation and

NOTE Confidence: 0.777480535833333

00:23:27.245 --> 00:23:29.190 the borderline, somewhat unclear.

NOTE Confidence: 0.777480535833333

00:23:29.190 --> 00:23:31.130 It's inflammatory infiltrate too

NOTE Confidence: 0.777480535833333

00:23:31.130 --> 00:23:33.990 sparse or mysite damage not apparent.

NOTE Confidence: 0.777480535833333

00:23:33.990 --> 00:23:35.985 So we don't know what's too few

NOTE Confidence: 0.777480535833333

00:23:35.985 --> 00:23:37.789 cells to call it borderline,

NOTE Confidence: 0.777480535833333

00:23:37.790 --> 00:23:40.030 what's too many cells to call it borderline,

NOTE Confidence: 0.777480535833333

00:23:40.030 --> 00:23:42.526 it's just kind of nebulous space.

NOTE Confidence: 0.777480535833333

00:23:42.530 --> 00:23:44.587 Again, this is published in 1986.

NOTE Confidence: 0.777480535833333

00:23:44.587 --> 00:23:46.969 And if you perform subsequent biopsies,

NOTE Confidence: 0.777480535833333

00:23:46.970 --> 00:23:48.650 which we tend not to do anymore,

NOTE Confidence: 0.777480535833333

00:23:48.650 --> 00:23:50.558 you could diagnose it as ongoing.

NOTE Confidence: 0.777480535833333

00:23:50.560 --> 00:23:52.378 Resolved for resolving,

NOTE Confidence: 0.777480535833333

00:23:52.378 --> 00:23:56.620 so I skipped one in the middle.

NOTE Confidence: 0.777480535833333

00:23:56.620 --> 00:24:01.480 In 2013, a second set of criteria came about.

NOTE Confidence: 0.777480535833333

00:24:01.480 --> 00:24:04.315 Where the key changes were now to

NOTE Confidence: 0.777480535833333

00:24:04.315 --> 00:24:05.696 introduce immunohistochemistry 1986,

NOTE Confidence: 0.777480535833333

00:24:05.696 --> 00:24:07.960 we weren't really doing

NOTE Confidence: 0.777480535833333

00:24:07.960 --> 00:24:09.398 immunohistochemistry frequently and

NOTE Confidence: 0.777480535833333

00:24:09.398 --> 00:24:11.568 certainly not on endomyocardial biopsy.

NOTE Confidence: 0.777480535833333

00:24:11.570 --> 00:24:13.360 So here a European group,

NOTE Confidence: 0.777480535833333

00:24:13.360 --> 00:24:15.250 the European Society of Cardiology.

NOTE Confidence: 0.766632917142857

00:24:18.280 --> 00:24:20.317 Made essentially 2 changes to the criteria.

NOTE Confidence: 0.766632917142857

00:24:20.320 --> 00:24:22.600 One was again to implement

NOTE Confidence: 0.766632917142857

00:24:22.600 --> 00:24:23.056 immunohistochemistry,

NOTE Confidence: 0.766632917142857

00:24:23.060 --> 00:24:25.088 looking for CD3 lymphocytes,

NOTE Confidence: 0.766632917142857

00:24:25.088 --> 00:24:28.130 and to define 14 leukocytes per

NOTE Confidence: 0.766632917142857

00:24:28.222 --> 00:24:31.026 millimeter squared as definitive

NOTE Confidence: 0.766632917142857

00:24:31.026 --> 00:24:33.338 diagnosis of myocarditis. OK.

NOTE Confidence: 0.766632917142857

00:24:33.338 --> 00:24:35.002 So that's the setting of what we have.

NOTE Confidence: 0.766632917142857

00:24:35.010 --> 00:24:36.898 We kind of have an old criteria that

NOTE Confidence: 0.766632917142857

00:24:36.898 --> 00:24:38.870 I thought everybody used and a new

NOTE Confidence: 0.766632917142857

00:24:38.870 --> 00:24:40.570 criteria that maybe some people use.

NOTE Confidence: 0.766632917142857

00:24:40.570 --> 00:24:42.646 Cause I actually wasn't using that.

NOTE Confidence: 0.766632917142857

00:24:42.650 --> 00:24:44.966 And we decided between the Society

NOTE Confidence: 0.766632917142857

00:24:44.966 --> 00:24:46.124 for Cardiovascular Pathology,

NOTE Confidence: 0.766632917142857

00:24:46.130 --> 00:24:48.750 SBP and the European Society,

NOTE Confidence: 0.766632917142857

00:24:48.750 --> 00:24:50.186 we should study this.

NOTE Confidence: 0.766632917142857

00:24:50.186 --> 00:24:51.981 We should find out what

NOTE Confidence: 0.766632917142857

00:24:51.981 --> 00:24:53.927 people are using as criteria.

NOTE Confidence: 0.766632917142857

00:24:53.930 --> 00:24:56.522 So this is now the work of Monica de

NOTE Confidence: 0.766632917142857

00:24:56.522 --> 00:24:58.858 Gaspari and Chi Lin and I worked with

NOTE Confidence: 0.766632917142857

00:24:58.858 --> 00:25:01.608 them where we developed a survey to ask

NOTE Confidence: 0.766632917142857

00:25:01.608 --> 00:25:03.774 people about how they diagnose myocarditis.

NOTE Confidence: 0.766632917142857

00:25:03.774 --> 00:25:05.718 We then sent emails out to

NOTE Confidence: 0.766632917142857

00:25:05.718 --> 00:25:07.758 members of both of our societies.

NOTE Confidence: 0.766632917142857

00:25:07.760 --> 00:25:08.928 We tweeted about it.

NOTE Confidence: 0.766632917142857

00:25:08.928 --> 00:25:11.402 I sent emails and other people sent directed

NOTE Confidence: 0.766632917142857

00:25:11.402 --> 00:25:14.058 emails to people to ask them to participate.

NOTE Confidence: 0.766632917142857

00:25:14.060 --> 00:25:16.046 And we were thrilled to get

NOTE Confidence: 0.766632917142857

00:25:16.046 --> 00:25:17.039 exactly 100 participants.

NOTE Confidence: 0.766632917142857

00:25:17.040 --> 00:25:19.308 It's so much easier to do math on 100

NOTE Confidence: 0.766632917142857

00:25:19.308 --> 00:25:22.080 than 101 or 99, and that was great.

NOTE Confidence: 0.766632917142857

00:25:22.080 --> 00:25:24.480 So we had 100 pathologists respond.

NOTE Confidence: 0.766632917142857

00:25:24.480 --> 00:25:25.845 You can see that half of them

NOTE Confidence: 0.766632917142857

00:25:25.845 --> 00:25:27.265 were from North America, roughly,

NOTE Confidence: 0.766632917142857

00:25:27.265 --> 00:25:29.935 and half were roughly from Europe.

NOTE Confidence: 0.766632917142857

00:25:29.940 --> 00:25:32.280 And a wide range of.

NOTE Confidence: 0.766632917142857

00:25:32.280 --> 00:25:34.614 Of sort of experience with heart

NOTE Confidence: 0.766632917142857

00:25:34.614 --> 00:25:37.353 biopsies from less than 10 think a

NOTE Confidence: 0.766632917142857

00:25:37.353 --> 00:25:39.573 reasonable chunk to greater than 200.

NOTE Confidence: 0.766632917142857

00:25:39.580 --> 00:25:43.136 And I have a colleague in Germany.

NOTE Confidence: 0.766632917142857

00:25:43.140 --> 00:25:44.440 Who Karen Klingle,

NOTE Confidence: 0.766632917142857

00:25:44.440 --> 00:25:47.240 who sees thousands of cases every year.

NOTE Confidence: 0.766632917142857

00:25:47.240 --> 00:25:48.446 She I think is the referral

NOTE Confidence: 0.766632917142857

00:25:48.446 --> 00:25:49.660 Center for all of Germany.

NOTE Confidence: 0.766632917142857

00:25:49.660 --> 00:25:52.412 So she has a huge cohort of cases and a lot

NOTE Confidence: 0.766632917142857

00:25:52.412 --> 00:25:54.876 of experience and she participated as well.

NOTE Confidence: 0.766632917142857

00:25:54.880 --> 00:25:56.424 So we started to ask this group questions

NOTE Confidence: 0.766632917142857

00:25:56.424 --> 00:25:57.919 and the first question we asked is,

NOTE Confidence: 0.766632917142857

00:25:57.920 --> 00:26:00.335 do we all use the same criteria?

NOTE Confidence: 0.766632917142857

00:26:00.340 --> 00:26:00.696 No,

NOTE Confidence: 0.766632917142857

00:26:00.696 --> 00:26:01.408 we don't.

NOTE Confidence: 0.766632917142857

00:26:01.408 --> 00:26:03.900 You can see that half the people

NOTE Confidence: 0.766632917142857

00:26:03.987 --> 00:26:06.467 use Dallas criteria exclusively,

NOTE Confidence: 0.766632917142857

00:26:06.470 --> 00:26:07.914 28 used both criteria,

NOTE Confidence: 0.766632917142857

00:26:07.914 --> 00:26:09.719 the European and Dallas criteria,

NOTE Confidence: 0.766632917142857

00:26:09.720 --> 00:26:10.880 and 12 claim to use.

NOTE Confidence: 0.766632917142857

00:26:10.880 --> 00:26:13.568 The European eight people didn't use either,

NOTE Confidence: 0.766632917142857

00:26:13.570 --> 00:26:15.148 and this was somewhat dependent on

NOTE Confidence: 0.766632917142857

00:26:15.148 --> 00:26:17.149 where in the world they were located.

NOTE Confidence: 0.766632917142857

00:26:17.150 --> 00:26:18.665 In North America,

NOTE Confidence: 0.766632917142857

00:26:18.665 --> 00:26:20.180 people predominantly use

NOTE Confidence: 0.766632917142857

00:26:20.180 --> 00:26:22.200 just the Dallas criteria,

NOTE Confidence: 0.766632917142857

00:26:22.200 --> 00:26:24.366 whereas in Europe they seem to

NOTE Confidence: 0.766632917142857

00:26:24.366 --> 00:26:27.213 mostly use your the ESC and then

NOTE Confidence: 0.766632917142857

00:26:27.213 --> 00:26:29.423 potentially Dallas criteria as well.

NOTE Confidence: 0.766632917142857

00:26:29.430 --> 00:26:31.120 So very much depends on.

NOTE Confidence: 0.766632917142857

00:26:31.120 --> 00:26:33.628 Where they were, we use criteria, no.

NOTE Confidence: 0.766632917142857

00:26:33.628 --> 00:26:35.182 What about immunohistochemistry

NOTE Confidence: 0.766632917142857

00:26:35.182 --> 00:26:37.254 and viral PCR studies?

NOTE Confidence: 0.766632917142857

00:26:37.260 --> 00:26:39.500 Do we use these consistently?

NOTE Confidence: 0.766632917142857

00:26:39.500 --> 00:26:39.980 No.

NOTE Confidence: 0.766632917142857

00:26:39.980 --> 00:26:40.460 OK,

NOTE Confidence: 0.766632917142857

00:26:40.460 --> 00:26:41.900 on the left,

NOTE Confidence: 0.766632917142857

00:26:41.900 --> 00:26:43.364 you see that half the European

NOTE Confidence: 0.766632917142857

00:26:43.364 --> 00:26:44.959 groups use IHC in every case,

NOTE Confidence: 0.766632917142857

00:26:44.960 --> 00:26:47.975 and the other group do it in selected cases.

NOTE Confidence: 0.766632917142857

00:26:47.980 --> 00:26:49.820 And in the United States,

NOTE Confidence: 0.766632917142857

00:26:49.820 --> 00:26:52.226 there's a group that do not

NOTE Confidence: 0.766632917142857

00:26:52.226 --> 00:26:53.028 perform immunohistochemistry

NOTE Confidence: 0.766632917142857

00:26:53.028 --> 00:26:55.299 on any cases for myocarditis.

NOTE Confidence: 0.766632917142857

00:26:55.300 --> 00:26:57.113 And I will tell you that my

NOTE Confidence: 0.766632917142857

00:26:57.113 --> 00:26:58.639 colleagues at the Mayo Clinic,

NOTE Confidence: 0.766632917142857

00:26:58.640 --> 00:27:00.292 who are some of the best cardiovascular

NOTE Confidence: 0.766632917142857

00:27:00.292 --> 00:27:01.360 pathologists in the country,

NOTE Confidence: 0.766632917142857

00:27:01.360 --> 00:27:03.024 don't use immunohistochemistry because

NOTE Confidence: 0.766632917142857

00:27:03.024 --> 00:27:06.160 it's not part of the Dallas criteria.

NOTE Confidence: 0.766632917142857

00:27:06.160 --> 00:27:08.195 I'll mention before that sometimes

NOTE Confidence: 0.766632917142857

00:27:08.195 --> 00:27:11.220 people use viral PCR to type viruses.

NOTE Confidence: 0.766632917142857

00:27:11.220 --> 00:27:12.640 Some people consider that an

NOTE Confidence: 0.766632917142857

00:27:12.640 --> 00:27:14.060 important part of the diagnosis,

NOTE Confidence: 0.766632917142857

00:27:14.060 --> 00:27:15.192 other people do not.

NOTE Confidence: 0.766632917142857

00:27:15.192 --> 00:27:15.758 In Europe,

NOTE Confidence: 0.834491297142857

00:27:15.760 --> 00:27:18.119 about half the groups routinely perform it,

NOTE Confidence: 0.834491297142857

00:27:18.120 --> 00:27:20.720 and North America's only 22%.

NOTE Confidence: 0.834491297142857

00:27:20.720 --> 00:27:22.730 At my institution, the pediatric team

NOTE Confidence: 0.834491297142857

00:27:22.730 --> 00:27:24.958 performs it and the adults do not.

NOTE Confidence: 0.834491297142857

00:27:24.960 --> 00:27:28.467 So even in one institution we have

NOTE Confidence: 0.834491297142857

00:27:28.467 --> 00:27:31.009 different approaches to doing this.

NOTE Confidence: 0.834491297142857

00:27:31.010 --> 00:27:33.234 Well, do we use the same terminology to

NOTE Confidence: 0.834491297142857

00:27:33.234 --> 00:27:35.730 all of us use at least the same terms?

NOTE Confidence: 0.834491297142857

00:27:35.730 --> 00:27:38.970 Again, no. You can see that giant cell

NOTE Confidence: 0.834491297142857

00:27:38.970 --> 00:27:41.240 myocarditis was the most commonly used

NOTE Confidence: 0.834491297142857

00:27:41.240 --> 00:27:44.140 term as like a top line diagnosis,

NOTE Confidence: 0.834491297142857

00:27:44.140 --> 00:27:45.832 you syphilitic myocarditis,

NOTE Confidence: 0.834491297142857

00:27:45.832 --> 00:27:48.088 lymphocytic myocarditis and down.

NOTE Confidence: 0.834491297142857

00:27:48.090 --> 00:27:50.415 But note that borderline myocarditis

NOTE Confidence: 0.834491297142857

00:27:50.415 --> 00:27:53.662 was used by 55% of the group.

NOTE Confidence: 0.834491297142857

00:27:53.662 --> 00:27:55.514 So that intermediate diagnosis

NOTE Confidence: 0.834491297142857

00:27:55.514 --> 00:27:57.829 wasn't even used by everyone.

NOTE Confidence: 0.834491297142857

00:27:57.830 --> 00:28:01.993 So this might be concerning, I don't know.

NOTE Confidence: 0.834491297142857

00:28:01.993 --> 00:28:03.919 Our conclusions were that there is

NOTE Confidence: 0.834491297142857

00:28:03.919 --> 00:28:06.338 not a consistent approach and the way

NOTE Confidence: 0.834491297142857

00:28:06.338 --> 00:28:08.689 we make the diagnosis of myocarditis,

NOTE Confidence: 0.834491297142857

00:28:08.690 --> 00:28:10.362 we have different criteria,

NOTE Confidence: 0.834491297142857

00:28:10.362 --> 00:28:12.452 we have different use of

NOTE Confidence: 0.834491297142857

00:28:12.452 --> 00:28:12.870 immunohistochemistry,

NOTE Confidence: 0.834491297142857

00:28:12.870 --> 00:28:15.089 different use of viral PCR and other

NOTE Confidence: 0.834491297142857

00:28:15.089 --> 00:28:17.831 things which I didn't bring up here, but.

NOTE Confidence: 0.834491297142857

00:28:17.831 --> 00:28:19.936 But maybe there's good news.

NOTE Confidence: 0.834491297142857

00:28:19.940 --> 00:28:21.596 What if it doesn't matter how

NOTE Confidence: 0.834491297142857

00:28:21.596 --> 00:28:23.410 we get to the diagnosis,

NOTE Confidence: 0.834491297142857

00:28:23.410 --> 00:28:25.466 it's so obvious that we all get to

NOTE Confidence: 0.834491297142857

00:28:25.466 --> 00:28:27.540 the same diagnosis no matter what.

NOTE Confidence: 0.834491297142857

00:28:27.540 --> 00:28:30.836 OK, so maybe this is like, you know,

NOTE Confidence: 0.834491297142857

00:28:30.836 --> 00:28:32.076 trying to thin slice something

NOTE Confidence: 0.834491297142857

00:28:32.076 --> 00:28:33.160 that doesn't really matter.

NOTE Confidence: 0.834491297142857

00:28:33.160 --> 00:28:34.275 We're going to anyone doesn't

NOTE Confidence: 0.834491297142857

00:28:34.275 --> 00:28:35.593 matter what criteria they use are

NOTE Confidence: 0.834491297142857

00:28:35.593 --> 00:28:36.720 going to see the slide and go,

NOTE Confidence: 0.834491297142857

00:28:36.720 --> 00:28:37.262 that's myocarditis.

NOTE Confidence: 0.834491297142857

00:28:37.262 --> 00:28:38.617 We're all going to agree.

NOTE Confidence: 0.834491297142857

00:28:38.620 --> 00:28:39.556 That's not myocarditis.

NOTE Confidence: 0.834491297142857

00:28:39.556 --> 00:28:41.428 We're all gonna agree and that

NOTE Confidence: 0.834491297142857

00:28:41.428 --> 00:28:42.260 would be great.

NOTE Confidence: 0.834491297142857

00:28:42.260 --> 00:28:44.648 So wouldn't a bunch of experts

NOTE Confidence: 0.834491297142857

00:28:44.648 --> 00:28:47.569 all agree on what is myocarditis?

NOTE Confidence: 0.834491297142857

00:28:47.570 --> 00:28:49.866 And so we did that experiment as well.

NOTE Confidence: 0.834491297142857

00:28:49.870 --> 00:28:52.633 Here I had the pleasure

NOTE Confidence: 0.834491297142857

00:28:52.633 --> 00:28:53.748 of working with Dan Liu,

NOTE Confidence: 0.834491297142857

00:28:53.750 --> 00:28:55.574 one of our trainees at Johns

NOTE Confidence: 0.834491297142857

00:28:55.574 --> 00:28:57.429 Hopkins where he blessed his heart,

NOTE Confidence: 0.834491297142857

00:28:57.430 --> 00:28:59.655 digitized 100 heart biopsy cases

NOTE Confidence: 0.834491297142857

00:28:59.655 --> 00:29:02.670 on a slick 6 slide scanner.

NOTE Confidence: 0.834491297142857

00:29:02.670 --> 00:29:04.536 These are diagnosis of cases that

NOTE Confidence: 0.834491297142857

00:29:04.536 --> 00:29:06.668 either myself or my colleague Charles

NOTE Confidence: 0.834491297142857

00:29:06.668 --> 00:29:09.134 Steenbergen had made at Johns Hopkins,

NOTE Confidence: 0.834491297142857

00:29:09.140 --> 00:29:12.180 31 cases of myocarditis 32 that we had

NOTE Confidence: 0.834491297142857

00:29:12.180 --> 00:29:14.730 diagnosed as borderline myocarditis,

NOTE Confidence: 0.834491297142857

00:29:14.730 --> 00:29:17.700 37 cases of non myocarditis.

NOTE Confidence: 0.834491297142857

00:29:17.700 --> 00:29:22.355 All cases had H&E's, usually four slides,

NOTE Confidence: 0.834491297142857

00:29:22.360 --> 00:29:23.740 CD3, CD 68 and a Mason,

NOTE Confidence: 0.834491297142857

00:29:23.740 --> 00:29:24.095 trichrome,

NOTE Confidence: 0.834491297142857

00:29:24.095 --> 00:29:26.580 that were all scanned and made available.

NOTE Confidence: 0.834491297142857

00:29:26.580 --> 00:29:29.135 We had a panel of eight international

NOTE Confidence: 0.834491297142857

00:29:29.135 --> 00:29:31.604 experts who were invited to independently

NOTE Confidence: 0.834491297142857

00:29:31.604 --> 00:29:34.214 provide a diagnosis on each case.

NOTE Confidence: 0.834491297142857

00:29:34.220 --> 00:29:36.166 They basically use the system I used

NOTE Confidence: 0.834491297142857

00:29:36.166 --> 00:29:38.140 this morning with the trainees proscia,

NOTE Confidence: 0.834491297142857

00:29:38.140 --> 00:29:40.576 just digital slides with a scoring sheet.

NOTE Confidence: 0.834491297142857

00:29:40.580 --> 00:29:42.360 The cases were all randomized.

NOTE Confidence: 0.834491297142857

00:29:42.360 --> 00:29:44.712 We told them only that everybody had

NOTE Confidence: 0.834491297142857

00:29:44.712 --> 00:29:47.179 a diagnosis of rule out myocarditis.

NOTE Confidence: 0.834491297142857

00:29:47.180 --> 00:29:48.780 Our plan was that they would have a

NOTE Confidence: 0.834491297142857

00:29:48.780 --> 00:29:50.540 lot of agreement where they didn't

NOTE Confidence: 0.834491297142857

00:29:50.540 --> 00:29:52.180 have agreement between the groups.

NOTE Confidence: 0.834491297142857

00:29:52.180 --> 00:29:54.140 We would resolve this maybe by e-mail.

NOTE Confidence: 0.834491297142857

00:29:54.140 --> 00:29:55.514 So let's say seven of eight

NOTE Confidence: 0.834491297142857

00:29:55.514 --> 00:29:57.080 agreed that it was myocarditis.

NOTE Confidence: 0.834491297142857

00:29:57.080 --> 00:29:58.556 One person said borderline would say,

NOTE Confidence: 0.834491297142857

00:29:58.560 --> 00:30:00.900 hey, everyone else is saying myocarditis.

NOTE Confidence: 0.834491297142857

00:30:00.900 --> 00:30:02.348 What do you think?

NOTE Confidence: 0.834491297142857

00:30:02.348 --> 00:30:04.940 If they said OK, we would say that's great.

NOTE Confidence: 0.834491297142857

00:30:04.940 --> 00:30:07.136 If they say, Nope, I'm sticking to my guns,

NOTE Confidence: 0.834491297142857

00:30:07.140 --> 00:30:08.204 we say, that's fine,

NOTE Confidence: 0.834491297142857

00:30:08.204 --> 00:30:09.800 we'll have a shared zoom session

NOTE Confidence: 0.834491297142857

00:30:09.854 --> 00:30:11.541 and we'll talk about all the cases

NOTE Confidence: 0.834491297142857

00:30:11.541 --> 00:30:13.070 that we don't have agreement.

NOTE Confidence: 0.834491297142857

00:30:13.070 --> 00:30:15.345 So 100 cases, it should be great.

NOTE Confidence: 0.85244914

00:30:15.350 --> 00:30:17.430 Nothing could go wrong.

NOTE Confidence: 0.85244914

00:30:17.430 --> 00:30:20.104 Well, it turned out that getting to

NOTE Confidence: 0.85244914

00:30:20.104 --> 00:30:22.548 consensus was really challenging to me.

NOTE Confidence: 0.85244914

00:30:22.550 --> 00:30:23.132 Surprisingly challenging.

NOTE Confidence: 0.85244914

00:30:23.132 --> 00:30:25.460 Although when I told the colleague he's like,

NOTE Confidence: 0.85244914

00:30:25.460 --> 00:30:27.444 why are you thinking this would be easy?

NOTE Confidence: 0.85244914

00:30:27.450 --> 00:30:28.443 I don't know.

NOTE Confidence: 0.85244914

00:30:28.443 --> 00:30:31.291 So this is the initial consensus to the

NOTE Confidence: 0.85244914

00:30:31.291 --> 00:30:34.069 Johns Hopkins signed out original diagnosis.

NOTE Confidence: 0.85244914

00:30:34.070 --> 00:30:35.718 They had full consensus.

NOTE Confidence: 0.85244914

00:30:35.718 --> 00:30:38.675 All eight people agreed on the on

NOTE Confidence: 0.85244914

00:30:38.675 --> 00:30:40.850 the diagnosis of borderline cases.

NOTE Confidence: 0.85244914

00:30:40.850 --> 00:30:44.516 Three 3 * 16 agreed on

NOTE Confidence: 0.85244914

00:30:44.516 --> 00:30:48.010 myocarditis cases 18 all agreed.

NOTE Confidence: 0.85244914

00:30:48.010 --> 00:30:49.306 On non myocarditis cases and I

NOTE Confidence: 0.85244914

00:30:49.306 --> 00:30:50.914 should go back for a moment and

NOTE Confidence: 0.85244914

00:30:50.914 --> 00:30:52.300 say for the non myocarditis cases,

NOTE Confidence: 0.85244914

00:30:52.300 --> 00:30:53.715 I was specifically looking for

NOTE Confidence: 0.85244914

00:30:53.715 --> 00:30:55.549 ones that I had reported as

NOTE Confidence: 0.85244914

00:30:55.549 --> 00:30:57.374 having a little more inflammatory

NOTE Confidence: 0.85244914

00:30:57.374 --> 00:30:58.834 infiltrate than complete baseline.

NOTE Confidence: 0.85244914

00:30:58.840 --> 00:31:01.724 So it made it a little harder.

NOTE Confidence: 0.85244914

00:31:01.730 --> 00:31:04.285 You see, for the three borderline cases,

NOTE Confidence: 0.85244914

00:31:04.290 --> 00:31:05.542 while they all agreed,

NOTE Confidence: 0.85244914

00:31:05.542 --> 00:31:07.107 they didn't agree with me,

NOTE Confidence: 0.85244914

00:31:07.110 --> 00:31:08.688 all these people, those three cases,

NOTE Confidence: 0.85244914

00:31:08.690 --> 00:31:10.790 everyone said this is not myocarditis.

NOTE Confidence: 0.85244914

00:31:10.790 --> 00:31:12.110 So they're basically saying, sorry,

NOTE Confidence: 0.85244914

00:31:12.110 --> 00:31:13.830 Mark, you blew that diagnosis,

NOTE Confidence: 0.85244914

00:31:13.830 --> 00:31:14.994 OK, that's fine.

NOTE Confidence: 0.85244914

00:31:14.994 --> 00:31:17.710 We had moderate diagnosis then on 13,

NOTE Confidence: 0.85244914

00:31:17.710 --> 00:31:20.702 nine and 13 cases where this was at

NOTE Confidence: 0.85244914

00:31:20.702 --> 00:31:23.947 least six of the eight people agreeing.

NOTE Confidence: 0.85244914

00:31:23.950 --> 00:31:25.987 And then we had 28 cases overall

NOTE Confidence: 0.85244914

00:31:25.987 --> 00:31:27.769 where there was low agreement.

NOTE Confidence: 0.85244914

00:31:27.770 --> 00:31:30.269 We had some cases where people said

NOTE Confidence: 0.85244914

00:31:30.269 --> 00:31:32.409 non myocarditis, some people said.

NOTE Confidence: 0.85244914

00:31:32.409 --> 00:31:35.247 Borderline markers and other people said

NOTE Confidence: 0.85244914

00:31:35.247 --> 00:31:37.349 myocarditis all on the same slides.

NOTE Confidence: 0.85244914

00:31:37.350 --> 00:31:39.166 And that was interesting.

NOTE Confidence: 0.85244914

00:31:39.166 --> 00:31:40.789 So we said, OK,

NOTE Confidence: 0.85244914

00:31:40.789 --> 00:31:41.048 we,

NOTE Confidence: 0.85244914

00:31:41.048 --> 00:31:43.120 we worked through this and we had a

NOTE Confidence: 0.85244914

00:31:43.185 --> 00:31:45.292 couple of big zoom sessions where we

NOTE Confidence: 0.85244914

00:31:45.292 --> 00:31:47.528 got people to try and work on this.

NOTE Confidence: 0.85244914

00:31:47.530 --> 00:31:49.906 It didn't get that much better.

NOTE Confidence: 0.85244914

00:31:49.910 --> 00:31:50.219 First,

NOTE Confidence: 0.85244914

00:31:50.219 --> 00:31:52.691 I discovered that two of my experts don't

NOTE Confidence: 0.85244914

00:31:52.691 --> 00:31:55.029 use the intermediate borderline term.

NOTE Confidence: 0.85244914

00:31:55.030 --> 00:31:57.704 So they were refusing to use the

NOTE Confidence: 0.85244914

00:31:57.704 --> 00:31:58.850 term borderline myocarditis.

NOTE Confidence: 0.85244914

00:31:58.850 --> 00:32:00.698 Now at least one of them had an

NOTE Confidence: 0.85244914

00:32:00.698 --> 00:32:02.147 intermediate term that they would use,

NOTE Confidence: 0.85244914

00:32:02.150 --> 00:32:03.910 which was like myocardium

NOTE Confidence: 0.85244914

00:32:03.910 --> 00:32:05.230 with increased inflammation.

NOTE Confidence: 0.85244914

00:32:05.230 --> 00:32:06.210 And I'd say, well,

NOTE Confidence: 0.85244914

00:32:06.210 --> 00:32:07.680 can't you just call that borderline?

NOTE Confidence: 0.85244914

00:32:07.680 --> 00:32:08.069 No,

NOTE Confidence: 0.85244914

00:32:08.069 --> 00:32:10.014 my clinicians like either yes

NOTE Confidence: 0.85244914

00:32:10.014 --> 00:32:12.519 or no for making the diagnosis

NOTE Confidence: 0.85244914

00:32:12.519 --> 00:32:14.694 of myocarditis and they're happy

NOTE Confidence: 0.85244914

00:32:14.694 --> 00:32:17.718 to try to please the clinician.

NOTE Confidence: 0.85244914

00:32:17.720 --> 00:32:20.440 We had 10 cases that were mostly borderline,

NOTE Confidence: 0.85244914

00:32:20.440 --> 00:32:22.060 which we achieved no consensus.

NOTE Confidence: 0.85244914

00:32:22.060 --> 00:32:24.076 We we sat around and talked about

NOTE Confidence: 0.85244914

00:32:24.076 --> 00:32:26.071 them and couldn't get everybody to

NOTE Confidence: 0.85244914

00:32:26.071 --> 00:32:28.207 agree whether it was borderline or

NOTE Confidence: 0.85244914

00:32:28.207 --> 00:32:30.037 myocarditis or borderline or nothing.

NOTE Confidence: 0.85244914

00:32:30.040 --> 00:32:31.876 And we we just dropped those

NOTE Confidence: 0.85244914

00:32:31.876 --> 00:32:33.100 cases and moved on.

NOTE Confidence: 0.85244914

00:32:33.100 --> 00:32:36.412 And then we had one case of borderline Plus,

NOTE Confidence: 0.85244914

00:32:36.420 --> 00:32:38.576 which is not even a real term.

NOTE Confidence: 0.85244914

00:32:38.580 --> 00:32:39.932 We just invented it so we could get

NOTE Confidence: 0.85244914

00:32:39.932 --> 00:32:41.548 to a consensus because everyone agreed

NOTE Confidence: 0.85244914

00:32:41.548 --> 00:32:43.093 to calling this borderline plus.

NOTE Confidence: 0.85244914

00:32:43.100 --> 00:32:45.424 But this is the Histology of that

NOTE Confidence: 0.85244914

00:32:45.424 --> 00:32:47.940 case and you can kind of see why.

NOTE Confidence: 0.85244914

00:32:47.940 --> 00:32:49.077 This was challenging.

NOTE Confidence: 0.85244914

00:32:49.077 --> 00:32:51.730 We had clearly collections of immune cells,

NOTE Confidence: 0.85244914

00:32:51.730 --> 00:32:52.579 way too many,

NOTE Confidence: 0.85244914

00:32:52.579 --> 00:32:54.560 although they are on the surface here

NOTE Confidence: 0.85244914

00:32:54.623 --> 00:32:56.423 we had collections that were inside

NOTE Confidence: 0.85244914

00:32:56.423 --> 00:32:58.350 the tissue of many lymphocytes.

NOTE Confidence: 0.85244914

00:32:58.350 --> 00:33:00.846 Here's a collection by CD3 and

NOTE Confidence: 0.85244914

00:33:00.846 --> 00:33:02.510 another collection of CD3.

NOTE Confidence: 0.85244914

00:33:02.510 --> 00:33:04.946 So clearly lots and lots of cells.

NOTE Confidence: 0.85244914

00:33:04.950 --> 00:33:07.194 Some people wanted to call this

NOTE Confidence: 0.85244914

00:33:07.194 --> 00:33:08.690 myocarditis even without injury

NOTE Confidence: 0.85244914

00:33:08.757 --> 00:33:10.815 and some people just wanted to

NOTE Confidence: 0.85244914

00:33:10.815 --> 00:33:11.844 call this borderline.

NOTE Confidence: 0.890533379583333

00:33:11.850 --> 00:33:13.074 So all of this.

NOTE Confidence: 0.890533379583333

00:33:13.074 --> 00:33:15.802 Was a bit of a problem because even

NOTE Confidence: 0.890533379583333

00:33:15.802 --> 00:33:18.623 my experts don't agree on how to

NOTE Confidence: 0.890533379583333

00:33:18.623 --> 00:33:21.447 make the diagnosis of myocarditis.

NOTE Confidence: 0.890533379583333

00:33:21.450 --> 00:33:23.274 So to kind of sum all this up,

NOTE Confidence: 0.890533379583333

00:33:23.280 --> 00:33:24.948 we really have challenges

NOTE Confidence: 0.890533379583333

00:33:24.948 --> 00:33:27.033 in the world of myocarditis.

NOTE Confidence: 0.890533379583333

00:33:27.040 --> 00:33:28.692 Cardiac MRI is good,

NOTE Confidence: 0.890533379583333

00:33:28.692 --> 00:33:30.757 but is not necessarily robust

NOTE Confidence: 0.890533379583333

00:33:30.757 --> 00:33:33.039 in all clinical scenarios.

NOTE Confidence: 0.890533379583333

00:33:33.040 --> 00:33:35.050 There are no specific clinical

NOTE Confidence: 0.890533379583333

00:33:35.050 --> 00:33:37.060 symptoms or lab findings that

NOTE Confidence: 0.890533379583333

00:33:37.134 --> 00:33:39.078 are specific for myocarditis.

NOTE Confidence: 0.890533379583333

00:33:39.080 --> 00:33:40.332 The micronite biomarker that

NOTE Confidence: 0.890533379583333

00:33:40.332 --> 00:33:42.500 was claimed is not a micro RNA,

NOTE Confidence: 0.890533379583333

00:33:42.500 --> 00:33:44.350 probably to definitely not a

NOTE Confidence: 0.890533379583333

00:33:44.350 --> 00:33:46.678 biomarker one in 2.5 billion chance.

NOTE Confidence: 0.890533379583333

00:33:46.678 --> 00:33:49.114 Not all pathologists use the same

NOTE Confidence: 0.890533379583333

00:33:49.114 --> 00:33:51.135 criteria to make the diagnosis

NOTE Confidence: 0.890533379583333

00:33:51.135 --> 00:33:53.065 of myocarditis and even experts

NOTE Confidence: 0.890533379583333

00:33:53.065 --> 00:33:55.229 don't agree on diagnosing cases,

NOTE Confidence: 0.890533379583333

00:33:55.230 --> 00:33:59.070 particularly the intermediate grade lesions.

NOTE Confidence: 0.890533379583333

00:33:59.070 --> 00:34:01.250 But where there are challenges,

NOTE Confidence: 0.890533379583333

00:34:01.250 --> 00:34:02.450 there are opportunities.

NOTE Confidence: 0.890533379583333

00:34:02.450 --> 00:34:05.710 So what can we do to improve this?

NOTE Confidence: 0.890533379583333

00:34:05.710 --> 00:34:07.564 The first thing we want to do is try

NOTE Confidence: 0.890533379583333

00:34:07.564 --> 00:34:09.586 and get the diagnostic criteria right.

NOTE Confidence: 0.890533379583333

00:34:09.590 --> 00:34:12.368 Can we improve the Dallas criteria?

NOTE Confidence: 0.890533379583333

00:34:12.370 --> 00:34:14.826 And the 2nd is to develop better tissue

NOTE Confidence: 0.890533379583333

00:34:14.826 --> 00:34:16.898 based methods to diagnose myocarditis.

NOTE Confidence: 0.890533379583333

00:34:16.900 --> 00:34:19.040 So those are going to be the last two parts.

NOTE Confidence: 0.890533379583333

00:34:19.040 --> 00:34:21.695 Of the talk and the first part is going

NOTE Confidence: 0.890533379583333

00:34:21.695 --> 00:34:24.317 to be revising the Dallas criteria.

NOTE Confidence: 0.890533379583333

00:34:24.320 --> 00:34:26.336 So let's talk about some opportunities

NOTE Confidence: 0.890533379583333

00:34:26.336 --> 00:34:28.240 to improve the Dallas criteria.

NOTE Confidence: 0.890533379583333

00:34:28.240 --> 00:34:29.736 We can incorporate immunohistochemistry,

NOTE Confidence: 0.890533379583333

00:34:29.736 --> 00:34:32.560 which is not part of the original.

NOTE Confidence: 0.890533379583333

00:34:32.560 --> 00:34:34.678 We can better define myocyte injury

NOTE Confidence: 0.890533379583333

00:34:34.678 --> 00:34:37.123 as very nebulous and the original

NOTE Confidence: 0.890533379583333

00:34:37.123 --> 00:34:39.055 diagnosis open to interpretation.

NOTE Confidence: 0.890533379583333

00:34:39.060 --> 00:34:41.538 We can improve thresholds for immune cells.

NOTE Confidence: 0.890533379583333

00:34:41.540 --> 00:34:43.878 How many cells is it to say

NOTE Confidence: 0.890533379583333

00:34:43.878 --> 00:34:44.880 this is borderline?

NOTE Confidence: 0.890533379583333

00:34:44.880 --> 00:34:47.835 How many is it say this is too many to be

NOTE Confidence: 0.890533379583333

00:34:47.835 --> 00:34:50.439 in some intermediate category or categories?

NOTE Confidence: 0.890533379583333

00:34:50.440 --> 00:34:53.499 Validate terms and diagnosis to outcome data.

NOTE Confidence: 0.890533379583333

00:34:53.500 --> 00:34:55.460 I think that's going to be important

NOTE Confidence: 0.890533379583333

00:34:55.460 --> 00:34:57.465 to show that these are meaningful

NOTE Confidence: 0.890533379583333

00:34:57.465 --> 00:35:00.027 descriptors that we're using and a separate

NOTE Confidence: 0.890533379583333

00:35:00.093 --> 00:35:02.098 diagnosis on biopsies from autopsy,

NOTE Confidence: 0.890533379583333

00:35:02.100 --> 00:35:02.966 explanted hearts.

NOTE Confidence: 0.890533379583333

00:35:02.966 --> 00:35:03.399 Again,

NOTE Confidence: 0.890533379583333

00:35:03.399 --> 00:35:05.997 Dallas criteria were designed for biopsies,

NOTE Confidence: 0.890533379583333

00:35:06.000 --> 00:35:08.118 but people have been using them

NOTE Confidence: 0.890533379583333

00:35:08.118 --> 00:35:09.530 incorrectly on autopsy hearts

NOTE Confidence: 0.890533379583333

00:35:09.593 --> 00:35:11.097 or maybe explanted hearts.

NOTE Confidence: 0.890533379583333

00:35:11.100 --> 00:35:15.140 Can we use terms or develop terms and

NOTE Confidence: 0.890533379583333

00:35:15.140 --> 00:35:17.958 criteria specifically for those specimens?

NOTE Confidence: 0.890533379583333

00:35:17.960 --> 00:35:20.440 So one of the things that I like

NOTE Confidence: 0.890533379583333

00:35:20.440 --> 00:35:22.508 to point out is back in 1986,

NOTE Confidence: 0.890533379583333

00:35:22.508 --> 00:35:24.972 it was a lot of experts sitting around

NOTE Confidence: 0.890533379583333

00:35:24.972 --> 00:35:26.843 looking at slides and didn't have a

NOTE Confidence: 0.890533379583333

00:35:26.843 --> 00:35:29.268 lot of data to base these criteria on.

NOTE Confidence: 0.890533379583333

00:35:29.270 --> 00:35:30.838 And we have a lot more data now.

NOTE Confidence: 0.890533379583333

00:35:30.840 --> 00:35:32.740 People have been talking about

NOTE Confidence: 0.890533379583333

00:35:32.740 --> 00:35:34.260 biopsies and evaluating biopsies

NOTE Confidence: 0.890533379583333

00:35:34.260 --> 00:35:36.230 and and reporting outcome data.

NOTE Confidence: 0.890533379583333

00:35:36.230 --> 00:35:37.928 And these are two examples that

NOTE Confidence: 0.890533379583333

00:35:37.928 --> 00:35:39.098 came out in 2022,

NOTE Confidence: 0.890533379583333

00:35:39.098 --> 00:35:41.006 which I think are really useful

NOTE Confidence: 0.890533379583333

00:35:41.006 --> 00:35:41.960 to think about.

NOTE Confidence: 0.890533379583333

00:35:41.960 --> 00:35:45.306 So this group in Spain had a

NOTE Confidence: 0.890533379583333

00:35:45.306 --> 00:35:47.466 paper that looked at biopsies.

NOTE Confidence: 0.890533379583333

00:35:47.466 --> 00:35:50.308 With a composite end event of heart

NOTE Confidence: 0.890533379583333

00:35:50.308 --> 00:35:51.927 transplant left ventricular assist

NOTE Confidence: 0.890533379583333

00:35:51.927 --> 00:35:54.489 device or death and so those are

NOTE Confidence: 0.890533379583333

00:35:54.489 --> 00:35:56.849 the two things panels on the left

NOTE Confidence: 0.890533379583333

00:35:56.849 --> 00:35:59.429 side here and this dark purple area.

NOTE Confidence: 0.890533379583333

00:35:59.429 --> 00:36:02.027 Those are individuals who are Dallas

NOTE Confidence: 0.890533379583333

00:36:02.027 --> 00:36:04.531 criteria positive and the blue is

NOTE Confidence: 0.890533379583333

00:36:04.531 --> 00:36:06.526 Dallas criteria negative and that

NOTE Confidence: 0.890533379583333

00:36:06.597 --> 00:36:09.434 added up to the 23% or so here.

NOTE Confidence: 0.890533379583333

00:36:09.434 --> 00:36:12.140 This is Dallas criteria negative or

NOTE Confidence: 0.890533379583333

00:36:12.231 --> 00:36:16.119 and or sorry Dallas positive and

NOTE Confidence: 0.890533379583333

00:36:16.119 --> 00:36:18.063 or immunohistochemistry positive.

NOTE Confidence: 0.890533379583333

00:36:18.070 --> 00:36:19.960 Suggesting that immune cells more

NOTE Confidence: 0.890533379583333

00:36:19.960 --> 00:36:21.850 immune cells than what sort

NOTE Confidence: 0.830093532272727

00:36:21.913 --> 00:36:24.181 of tolerated as myocarditis and Dallas

NOTE Confidence: 0.830093532272727

00:36:24.181 --> 00:36:26.500 are meaningful to that bad outcome.

NOTE Confidence: 0.830093532272727

00:36:26.500 --> 00:36:28.792 So you don't have to necessarily

NOTE Confidence: 0.830093532272727

00:36:28.792 --> 00:36:30.973 see myocarditis with injury to get

NOTE Confidence: 0.830093532272727

00:36:30.973 --> 00:36:32.731 to a biopsy where that patient

NOTE Confidence: 0.830093532272727

00:36:32.731 --> 00:36:34.718 is going to have that outcome.

NOTE Confidence: 0.830093532272727

00:36:34.720 --> 00:36:36.603 I think that same data is supported

NOTE Confidence: 0.830093532272727

00:36:36.603 --> 00:36:39.049 here from a paper out of Japan and

NOTE Confidence: 0.830093532272727

00:36:39.049 --> 00:36:40.624 Cirque Journal where they looked

NOTE Confidence: 0.830093532272727

00:36:40.687 --> 00:36:43.536 at people who had what they called

NOTE Confidence: 0.830093532272727

00:36:43.536 --> 00:36:44.757 inflammatory dilated cardiomyopathy,

NOTE Confidence: 0.830093532272727

00:36:44.760 --> 00:36:46.489 meaning they saw too many immune cells

NOTE Confidence: 0.830093532272727

00:36:46.489 --> 00:36:48.499 in the setting of dilated cardiomyopathy.

NOTE Confidence: 0.830093532272727

00:36:48.500 --> 00:36:50.817 Which is probably very similar or the

NOTE Confidence: 0.830093532272727

00:36:50.817 --> 00:36:53.369 same thing as borderline myocarditis.

NOTE Confidence: 0.830093532272727

00:36:53.370 --> 00:36:56.466 And where they had more CD3 positive cells,

NOTE Confidence: 0.830093532272727

00:36:56.470 --> 00:36:58.490 those patients had worse outcomes,

NOTE Confidence: 0.830093532272727

00:36:58.490 --> 00:37:01.290 less survival free of cardiac death or

NOTE Confidence: 0.830093532272727

00:37:01.290 --> 00:37:03.889 left ventricular cyst device implantation.

NOTE Confidence: 0.830093532272727

00:37:03.890 --> 00:37:05.350 Where they saw fewer cells,

NOTE Confidence: 0.830093532272727

00:37:05.350 --> 00:37:06.694 those patients did better.

NOTE Confidence: 0.830093532272727

00:37:06.694 --> 00:37:09.547 Now note, it did take about 9 years to

NOTE Confidence: 0.830093532272727

00:37:09.547 --> 00:37:12.230 see like these really big differences.

NOTE Confidence: 0.830093532272727

00:37:12.230 --> 00:37:14.330 That's just a pretty long prediction

NOTE Confidence: 0.830093532272727

00:37:14.330 --> 00:37:15.030 in advance,

NOTE Confidence: 0.830093532272727

00:37:15.030 --> 00:37:17.144 but it does tell us that more

NOTE Confidence: 0.830093532272727

00:37:17.144 --> 00:37:18.510 immune cells are worse.

NOTE Confidence: 0.830093532272727

00:37:18.510 --> 00:37:19.044 And fewer.

NOTE Confidence: 0.830093532272727

00:37:19.044 --> 00:37:20.646 So it's something we should be

NOTE Confidence: 0.830093532272727

00:37:20.646 --> 00:37:22.518 cognizant of when we make new criteria,

NOTE Confidence: 0.830093532272727

00:37:22.520 --> 00:37:26.276 not look to lump everything together.

NOTE Confidence: 0.830093532272727

00:37:26.280 --> 00:37:29.700 So we decided to go after this and these

NOTE Confidence: 0.830093532272727

00:37:29.700 --> 00:37:33.537 are the goals that we set up for ourselves,

NOTE Confidence: 0.830093532272727

00:37:33.540 --> 00:37:35.628 very similar to what the opportunities

NOTE Confidence: 0.830093532272727

00:37:35.628 --> 00:37:37.804 were to develop revised biopsy criteria

NOTE Confidence: 0.830093532272727

00:37:37.804 --> 00:37:40.338 for a better definition of myocyte injury,

NOTE Confidence: 0.830093532272727

00:37:40.340 --> 00:37:42.440 better incorporation of immunohistochemistry,

NOTE Confidence: 0.830093532272727

00:37:42.440 --> 00:37:45.590 better classification based on the extent

NOTE Confidence: 0.830093532272727

00:37:45.654 --> 00:37:47.644 of injury and better classification

NOTE Confidence: 0.830093532272727

00:37:47.644 --> 00:37:49.634 based on types of myocarditis.

NOTE Confidence: 0.830093532272727

00:37:49.640 --> 00:37:51.644 So that's what we're doing on

NOTE Confidence: 0.830093532272727

00:37:51.644 --> 00:37:52.646 the biopsy side.

NOTE Confidence: 0.830093532272727

00:37:52.650 --> 00:37:55.236 On the autopsy or explant side,

NOTE Confidence: 0.830093532272727

00:37:55.240 --> 00:37:56.284 it's to define.

NOTE Confidence: 0.830093532272727

00:37:56.284 --> 00:37:58.372 Carditis based on evaluation of the

NOTE Confidence: 0.830093532272727

00:37:58.372 --> 00:38:00.731 whole heart and to synergize this

NOTE Confidence: 0.830093532272727

00:38:00.731 --> 00:38:02.681 terminology with the biopsy criteria

NOTE Confidence: 0.830093532272727

00:38:02.749 --> 00:38:05.227 and ultimately it's to validate all of

NOTE Confidence: 0.830093532272727

00:38:05.227 --> 00:38:08.870 these criteria with historical samples.

NOTE Confidence: 0.830093532272727

00:38:08.870 --> 00:38:11.383 And so the timeline that we've been

NOTE Confidence: 0.830093532272727

00:38:11.383 --> 00:38:13.992 working on is here in March of 2023,

NOTE Confidence: 0.830093532272727

00:38:13.992 --> 00:38:16.248 we met at the use CAP meeting and

NOTE Confidence: 0.830093532272727

00:38:16.248 --> 00:38:18.524 developed consensus that we wanted to go

NOTE Confidence: 0.830093532272727

00:38:18.524 --> 00:38:20.800 forward with revising the Dallas criteria.

NOTE Confidence: 0.830093532272727

00:38:20.800 --> 00:38:23.313 The SVP and the European Society both

NOTE Confidence: 0.830093532272727

00:38:23.313 --> 00:38:26.399 agreed that we should go forward with this.

NOTE Confidence: 0.830093532272727

00:38:26.400 --> 00:38:29.438 We then created 210 person teams to

NOTE Confidence: 0.830093532272727

00:38:29.438 --> 00:38:32.349 work on generating these new criteria.

NOTE Confidence: 0.830093532272727

00:38:32.350 --> 00:38:33.850 It started with the literature review.

NOTE Confidence: 0.830093532272727

00:38:33.850 --> 00:38:35.250 I showed you a couple of examples,

NOTE Confidence: 0.830093532272727

00:38:35.250 --> 00:38:37.590 but we grabbed hunt, not hundreds,

NOTE Confidence: 0.830093532272727

00:38:37.590 --> 00:38:38.850 that's too many, but.

NOTE Confidence: 0.830093532272727

00:38:38.850 --> 00:38:40.740 Scores and scores of papers that

NOTE Confidence: 0.830093532272727

00:38:40.801 --> 00:38:41.560 we then read,

NOTE Confidence: 0.830093532272727

00:38:41.560 --> 00:38:44.130 evaluated and sort of discussed

NOTE Confidence: 0.830093532272727

00:38:44.130 --> 00:38:45.158 amongst ourselves.

NOTE Confidence: 0.830093532272727

00:38:45.160 --> 00:38:46.894 We then did an adelphic question

NOTE Confidence: 0.830093532272727

00:38:46.894 --> 00:38:49.075 and answer where we took like the

NOTE Confidence: 0.830093532272727

00:38:49.075 --> 00:38:50.675 key questions related to biopsy,

NOTE Confidence: 0.830093532272727

00:38:50.680 --> 00:38:52.768 sent them out to everybody in the group

NOTE Confidence: 0.830093532272727

00:38:52.768 --> 00:38:55.019 and got everyone's anonymous feedback.

NOTE Confidence: 0.830093532272727

00:38:55.020 --> 00:38:58.524 And then saw what sort of where people

NOTE Confidence: 0.830093532272727

00:38:58.524 --> 00:39:01.209 were based on their own beliefs

NOTE Confidence: 0.830093532272727

00:39:01.209 --> 00:39:03.375 and experiences and ask people to

NOTE Confidence: 0.830093532272727

00:39:03.375 --> 00:39:05.350 find the data that supported it.

NOTE Confidence: 0.830093532272727

00:39:05.350 --> 00:39:07.036 Because if this is not data-driven,

NOTE Confidence: 0.830093532272727

00:39:07.040 --> 00:39:10.024 it's probably not worth doing in my opinion.

NOTE Confidence: 0.830093532272727

00:39:10.030 --> 00:39:12.536 Our goal is to have preliminary criteria

NOTE Confidence: 0.830093532272727

00:39:12.536 --> 00:39:15.100 for both of these by March of 2023.

NOTE Confidence: 0.830093532272727

00:39:15.100 --> 00:39:16.350 And on the biopsy side,

NOTE Confidence: 0.830093532272727

00:39:16.350 --> 00:39:18.276 we've already split into three or

NOTE Confidence: 0.830093532272727

00:39:18.276 --> 00:39:20.164 four groups to work on criteria

NOTE Confidence: 0.830093532272727

00:39:20.164 --> 00:39:22.234 ideas independently which we're going

NOTE Confidence: 0.830093532272727

00:39:22.234 --> 00:39:24.760 to bring together and have by the

NOTE Confidence: 0.830093532272727

00:39:24.760 --> 00:39:26.636 use CAP meeting and then spend a

NOTE Confidence: 0.81884808826087

00:39:26.700 --> 00:39:27.978 year evaluating this.

NOTE Confidence: 0.81884808826087

00:39:27.980 --> 00:39:30.140 We want to kick the tires on these criteria.

NOTE Confidence: 0.81884808826087

00:39:30.140 --> 00:39:32.748 We're going to go back to historical data,

NOTE Confidence: 0.81884808826087

00:39:32.750 --> 00:39:33.798 Johns Hopkins Place where

NOTE Confidence: 0.81884808826087

00:39:33.798 --> 00:39:35.108 we have historically done a

NOTE Confidence: 0.81884808826087

00:39:35.108 --> 00:39:36.528 lot of MRI cardiac biopsies.

NOTE Confidence: 0.81884808826087

00:39:36.530 --> 00:39:38.714 I mentioned Karen Klingle and Germany

NOTE Confidence: 0.81884808826087

00:39:38.714 --> 00:39:41.560 having so many cases you wouldn't believe.

NOTE Confidence: 0.81884808826087

00:39:41.560 --> 00:39:44.185 And seeing if the criteria that we've

NOTE Confidence: 0.81884808826087

00:39:44.185 --> 00:39:46.602 generated with have meaningful outcome or

NOTE Confidence: 0.81884808826087

00:39:46.602 --> 00:39:49.458 usefulness relative to where we are now.

NOTE Confidence: 0.81884808826087

00:39:49.460 --> 00:39:51.556 And some of the things that we've been

NOTE Confidence: 0.81884808826087

00:39:51.556 --> 00:39:53.517 playing with are in the Dallas criteria,

NOTE Confidence: 0.81884808826087

00:39:53.520 --> 00:39:55.092 expanding that borderline myocarditis

NOTE Confidence: 0.81884808826087

00:39:55.092 --> 00:39:58.279 to maybe a low and a high number

NOTE Confidence: 0.81884808826087

00:39:58.279 --> 00:39:59.416 of immune cells,

NOTE Confidence: 0.81884808826087

00:39:59.420 --> 00:40:01.412 better defining whether these are diffuse

NOTE Confidence: 0.81884808826087

00:40:01.412 --> 00:40:03.598 immune cells or clusters of immune cells.

NOTE Confidence: 0.81884808826087

00:40:03.600 --> 00:40:05.427 But these are all things we need

NOTE Confidence: 0.81884808826087

00:40:05.427 --> 00:40:06.961 to really evaluate and see how

NOTE Confidence: 0.81884808826087

00:40:06.961 --> 00:40:08.359 they're going to work for us.

NOTE Confidence: 0.81884808826087

00:40:08.360 --> 00:40:10.004 And then in March of 2024,

NOTE Confidence: 0.81884808826087

00:40:10.004 --> 00:40:11.708 again in conjunction with the use.

NOTE Confidence: 0.81884808826087

00:40:11.710 --> 00:40:12.815 That meeting which is going

NOTE Confidence: 0.81884808826087

00:40:12.815 --> 00:40:13.699 to be in Baltimore,

NOTE Confidence: 0.81884808826087

00:40:13.700 --> 00:40:16.157 we're gonna have a one day event

NOTE Confidence: 0.81884808826087

00:40:16.157 --> 00:40:17.983 to hopefully introduce the criteria

NOTE Confidence: 0.81884808826087

00:40:17.983 --> 00:40:20.440 to the larger world and take last

NOTE Confidence: 0.81884808826087

00:40:20.440 --> 00:40:22.457 feedback on them from a wider

NOTE Confidence: 0.81884808826087

00:40:22.457 --> 00:40:24.368 audience as whether these are useful.

NOTE Confidence: 0.81884808826087

00:40:24.368 --> 00:40:26.216 So all this is to say,

NOTE Confidence: 0.81884808826087

00:40:26.220 --> 00:40:27.810 we've been using the Dallas criteria

NOTE Confidence: 0.81884808826087

00:40:27.810 --> 00:40:30.143 for far too long and we are finally

NOTE Confidence: 0.81884808826087

00:40:30.143 --> 00:40:31.668 getting around to optimizing and

NOTE Confidence: 0.81884808826087

00:40:31.668 --> 00:40:33.143 improving them and we're very

NOTE Confidence: 0.81884808826087

00:40:33.143 --> 00:40:33.980 excited about this,

NOTE Confidence: 0.81884808826087

00:40:33.980 --> 00:40:37.228 what we hope is a good change

NOTE Confidence: 0.81884808826087

00:40:37.228 --> 00:40:39.720 for myocarditis. Now.

NOTE Confidence: 0.81884808826087

00:40:39.720 --> 00:40:42.180 That's one thing that we're doing.

NOTE Confidence: 0.81884808826087

00:40:42.180 --> 00:40:44.852 The next last thing I want to talk

NOTE Confidence: 0.81884808826087

00:40:44.852 --> 00:40:46.935 about is diagnosing myocarditis

NOTE Confidence: 0.81884808826087

00:40:46.935 --> 00:40:48.939 beyond immune cells.

NOTE Confidence: 0.81884808826087

00:40:48.940 --> 00:40:50.626 And what I really haven't mentioned

NOTE Confidence: 0.81884808826087

00:40:50.626 --> 00:40:52.691 so far is that myocarditis is

NOTE Confidence: 0.81884808826087

00:40:52.691 --> 00:40:54.008 a heterogeneous disease.

NOTE Confidence: 0.81884808826087

00:40:54.010 --> 00:40:56.206 And so when sometimes when that

NOTE Confidence: 0.81884808826087

00:40:56.206 --> 00:40:57.304 endomyocardial biopsy plucks

NOTE Confidence: 0.81884808826087

00:40:57.304 --> 00:40:59.111 those little bits of tissue from

NOTE Confidence: 0.81884808826087

00:40:59.111 --> 00:41:00.496 the side of the septum,

NOTE Confidence: 0.81884808826087

00:41:00.500 --> 00:41:03.180 it might miss that infiltrate.

NOTE Confidence: 0.81884808826087

00:41:03.180 --> 00:41:05.378 So The Dirty little secret in biopsying

NOTE Confidence: 0.81884808826087

00:41:05.378 --> 00:41:07.848 is we're only good at finding myocarditis

NOTE Confidence: 0.81884808826087

00:41:07.848 --> 00:41:09.780 about 50% of the time when it's there.

NOTE Confidence: 0.81884808826087

00:41:09.780 --> 00:41:12.210 And this is based on a study where they

NOTE Confidence: 0.81884808826087

00:41:12.210 --> 00:41:14.757 took autopsy hearts that had myocarditis,

NOTE Confidence: 0.81884808826087

00:41:14.760 --> 00:41:16.832 took a case bioptome and pulled little

NOTE Confidence: 0.81884808826087

00:41:16.832 --> 00:41:19.456 pieces off the septum and saw how frequently.

NOTE Confidence: 0.81884808826087

00:41:19.460 --> 00:41:21.434 They can make the diagnosis and

NOTE Confidence: 0.81884808826087

00:41:21.434 --> 00:41:23.459 actually the more pieces the better.

NOTE Confidence: 0.81884808826087

00:41:23.460 --> 00:41:25.080 5 being better than three.

NOTE Confidence: 0.81884808826087

00:41:25.080 --> 00:41:25.626 My institution,

NOTE Confidence: 0.81884808826087

00:41:25.626 --> 00:41:26.718 they give me 3.

NOTE Confidence: 0.81884808826087

00:41:26.720 --> 00:41:29.106 So maybe we're only 30% good at

NOTE Confidence: 0.81884808826087

00:41:29.106 --> 00:41:29.752 finding myocarditis.

NOTE Confidence: 0.81884808826087

00:41:29.752 --> 00:41:32.637 So it is a problem because we can miss it.

NOTE Confidence: 0.81884808826087

00:41:32.640 --> 00:41:35.232 We could be just next to it and miss

NOTE Confidence: 0.81884808826087

00:41:35.232 --> 00:41:38.041 it or what we're calling borderline

NOTE Confidence: 0.81884808826087

00:41:38.041 --> 00:41:41.300 myocarditis could be really close to injury,

NOTE Confidence: 0.81884808826087

00:41:41.300 --> 00:41:43.076 but always here a few cells,

NOTE Confidence: 0.81884808826087

00:41:43.080 --> 00:41:44.400 but also for borderline.

NOTE Confidence: 0.81884808826087

00:41:44.400 --> 00:41:46.380 And I didn't say this before,

NOTE Confidence: 0.81884808826087

00:41:46.380 --> 00:41:48.532 anybody of my age or older is going

NOTE Confidence: 0.81884808826087

00:41:48.532 --> 00:41:50.898 to have a collection of lymphocytes.

NOTE Confidence: 0.81884808826087

00:41:50.900 --> 00:41:51.900 Somewhere in their heart.

NOTE Confidence: 0.81884808826087

00:41:51.900 --> 00:41:53.400 If you take enough samples of

NOTE Confidence: 0.81884808826087

00:41:53.455 --> 00:41:54.547 someone's heart over 50,

NOTE Confidence: 0.81884808826087

00:41:54.550 --> 00:41:55.768 you're going to see a collection.

NOTE Confidence: 0.81884808826087

00:41:55.770 --> 00:41:56.862 Is that meaningful?

NOTE Confidence: 0.81884808826087

00:41:56.862 --> 00:41:57.590 Probably not.

NOTE Confidence: 0.81884808826087

00:41:57.590 --> 00:41:59.802 So it's either a random collection that

NOTE Confidence: 0.81884808826087

00:41:59.802 --> 00:42:02.128 you bump into by accident on biopsy,

NOTE Confidence: 0.81884808826087

00:42:02.130 --> 00:42:04.866 or is the tip of the iceberg and

NOTE Confidence: 0.81884808826087

00:42:04.866 --> 00:42:07.578 you're just missing something nearby.

NOTE Confidence: 0.81884808826087

00:42:07.580 --> 00:42:10.380 So what we've started to think about is,

NOTE Confidence: 0.81884808826087

00:42:10.380 --> 00:42:12.172 let's say this is a biopsy that

NOTE Confidence: 0.81884808826087

00:42:12.172 --> 00:42:12.940 was performed this

NOTE Confidence: 0.878341105833333

00:42:12.996 --> 00:42:15.860 number one, and that star represents an

NOTE Confidence: 0.878341105833333

00:42:15.860 --> 00:42:18.780 area of inflammation and myocyte injury.

NOTE Confidence: 0.878341105833333

00:42:18.780 --> 00:42:20.778 If you biopsy that by Histology,

NOTE Confidence: 0.878341105833333

00:42:20.780 --> 00:42:22.100 you're going to be able

NOTE Confidence: 0.878341105833333

00:42:22.100 --> 00:42:23.156 to make the diagnosis.

NOTE Confidence: 0.878341105833333

00:42:23.160 --> 00:42:25.435 But we also suspect that the cells,

NOTE Confidence: 0.878341105833333

00:42:25.440 --> 00:42:27.414 the native cells in the heart

NOTE Confidence: 0.878341105833333

00:42:27.414 --> 00:42:29.197 are probably responding to that

NOTE Confidence: 0.878341105833333

00:42:29.197 --> 00:42:30.797 immune infiltrate and injury.

NOTE Confidence: 0.878341105833333

00:42:30.800 --> 00:42:32.468 The myocytes themselves,

NOTE Confidence: 0.878341105833333

00:42:32.468 --> 00:42:34.136 the endothelial cells,

NOTE Confidence: 0.878341105833333

00:42:34.140 --> 00:42:35.202 the native fibroblasts,

NOTE Confidence: 0.878341105833333

00:42:35.202 --> 00:42:38.165 they may be sensing this damage in this

NOTE Confidence: 0.878341105833333

00:42:38.165 --> 00:42:40.679 process and changing their signaling state.

NOTE Confidence: 0.878341105833333

00:42:40.680 --> 00:42:42.878 And the question is can we identify

NOTE Confidence: 0.878341105833333

00:42:42.878 --> 00:42:45.250 what that is and can we capture

NOTE Confidence: 0.878341105833333

00:42:45.250 --> 00:42:47.290 that information so if we instead

NOTE Confidence: 0.878341105833333

00:42:47.363 --> 00:42:49.589 of biopsying this piece of tissue?

NOTE Confidence: 0.878341105833333

00:42:49.590 --> 00:42:51.720 I'm biopsying this piece of tissue,

NOTE Confidence: 0.878341105833333

00:42:51.720 --> 00:42:53.460 but whatever this process is,

NOTE Confidence: 0.878341105833333

00:42:53.460 --> 00:42:55.110 is sending out a signal

NOTE Confidence: 0.878341105833333

00:42:55.110 --> 00:42:56.760 really wide out to here.

NOTE Confidence: 0.878341105833333

00:42:56.760 --> 00:42:59.560 Maybe I can still sense that signal

NOTE Confidence: 0.878341105833333

00:42:59.560 --> 00:43:01.779 adjacent that's going to increase

NOTE Confidence: 0.878341105833333

00:43:01.779 --> 00:43:04.134 our yield on endomyocardial biopsy.

NOTE Confidence: 0.878341105833333

00:43:04.140 --> 00:43:06.219 Now this won't be necessary for cases

NOTE Confidence: 0.878341105833333

00:43:06.219 --> 00:43:08.141 where very obvious myocarditis could be

NOTE Confidence: 0.878341105833333

00:43:08.141 --> 00:43:10.409 rendered even if my experts don't agree,

NOTE Confidence: 0.878341105833333

00:43:10.410 --> 00:43:11.586 but can get close.

NOTE Confidence: 0.878341105833333

00:43:11.586 --> 00:43:13.350 It will be useful in scenarios

NOTE Confidence: 0.878341105833333

00:43:13.416 --> 00:43:15.360 where there is a borderline type

NOTE Confidence: 0.878341105833333

00:43:15.360 --> 00:43:17.371 of diagnosis where we see some

NOTE Confidence: 0.878341105833333

00:43:17.371 --> 00:43:19.315 inflammation but don't see enough to

NOTE Confidence: 0.878341105833333

00:43:19.315 --> 00:43:21.089 make the diagnosis of myocarditis.

NOTE Confidence: 0.878341105833333

00:43:21.089 --> 00:43:23.327 Or in certain clinical scenarios where

NOTE Confidence: 0.878341105833333

00:43:23.327 --> 00:43:25.570 the suspicion is very high and again,

NOTE Confidence: 0.878341105833333

00:43:25.570 --> 00:43:29.259 we might have just missed that material.

NOTE Confidence: 0.878341105833333

00:43:29.260 --> 00:43:31.752 Now this has probably been a long

NOTE Confidence: 0.878341105833333

00:43:31.752 --> 00:43:34.420 standing dream for a for years and

NOTE Confidence: 0.878341105833333

00:43:34.420 --> 00:43:36.335 it's known that cardiac myocytes

NOTE Confidence: 0.878341105833333

00:43:36.335 --> 00:43:38.570 respond to inflammation and induce

NOTE Confidence: 0.878341105833333

00:43:38.570 --> 00:43:41.240 their own cytokines to cardiac injury.

NOTE Confidence: 0.878341105833333

00:43:41.240 --> 00:43:42.983 As you can see in this nice

NOTE Confidence: 0.878341105833333

00:43:42.983 --> 00:43:44.359 review from some years ago.

NOTE Confidence: 0.878341105833333

00:43:44.360 --> 00:43:47.372 And this is a paper from 2004 showing

NOTE Confidence: 0.878341105833333

00:43:47.372 --> 00:43:50.424 that tissue necrosis factor alpha or TNF

NOTE Confidence: 0.878341105833333

00:43:50.424 --> 00:43:53.379 alpha is increased in cardiac myocytes.

NOTE Confidence: 0.878341105833333

00:43:53.380 --> 00:43:55.214 So you can see that here and

NOTE Confidence: 0.878341105833333

00:43:55.214 --> 00:43:57.414 that's sort of a sign that these

NOTE Confidence: 0.878341105833333

00:43:57.414 --> 00:43:59.104 cells are changing their immune.

NOTE Confidence: 0.878341105833333

00:43:59.110 --> 00:43:59.547 Response.

NOTE Confidence: 0.878341105833333

00:43:59.547 --> 00:44:00.421 However, historically,

NOTE Confidence: 0.878341105833333

00:44:00.421 --> 00:44:03.480 if we wanted to look for differences

NOTE Confidence: 0.878341105833333

00:44:03.550 --> 00:44:05.770 between disease and normal tissues,

NOTE Confidence: 0.878341105833333

00:44:05.770 --> 00:44:06.822 we get the tissues,

NOTE Confidence: 0.878341105833333

00:44:06.822 --> 00:44:07.874 we grind it up,

NOTE Confidence: 0.878341105833333

00:44:07.880 --> 00:44:09.866 we look for gene expression differences,

NOTE Confidence: 0.878341105833333

00:44:09.870 --> 00:44:10.544 very straightforward.

NOTE Confidence: 0.878341105833333

00:44:10.544 --> 00:44:13.240 But if you have a lot of immune

NOTE Confidence: 0.878341105833333

00:44:13.309 --> 00:44:14.710 cells infiltrating in,

NOTE Confidence: 0.878341105833333

00:44:14.710 --> 00:44:16.408 that big immune signal you're going

NOTE Confidence: 0.878341105833333

00:44:16.408 --> 00:44:18.526 to see is really mostly coming from

NOTE Confidence: 0.878341105833333

00:44:18.526 --> 00:44:20.696 those immune cells and you're going to

NOTE Confidence: 0.878341105833333

00:44:20.754 --> 00:44:22.776 be missing the more subtle potentially

NOTE Confidence: 0.878341105833333

00:44:22.776 --> 00:44:25.550 signals that are coming from myocytes,

NOTE Confidence: 0.878341105833333

00:44:25.550 --> 00:44:26.260 fibroblasts,

NOTE Confidence: 0.878341105833333

00:44:26.260 --> 00:44:28.390 endothelial cells relative.

NOTE Confidence: 0.878341105833333

00:44:28.390 --> 00:44:30.466 So that's always been a challenge

NOTE Confidence: 0.878341105833333

00:44:30.466 --> 00:44:31.850 we can't really assign.

NOTE Confidence: 0.878341105833333

00:44:31.850 --> 00:44:33.670 Those signals to this the

NOTE Confidence: 0.878341105833333

00:44:33.670 --> 00:44:35.800 cells we want to look at.

NOTE Confidence: 0.878341105833333

00:44:35.800 --> 00:44:37.720 So that's where spatial transcriptomics

NOTE Confidence: 0.878341105833333

00:44:37.720 --> 00:44:39.640 can potentially help us out.

NOTE Confidence: 0.878341105833333

00:44:39.640 --> 00:44:39.956 OK.

NOTE Confidence: 0.878341105833333

00:44:39.956 --> 00:44:42.168 So we have started to do some

NOTE Confidence: 0.878341105833333

00:44:42.168 --> 00:44:43.977 work in collaboration with

NOTE Confidence: 0.878341105833333

00:44:43.977 --> 00:44:46.727 Luigi Adamo and Kevin Partilla.

NOTE Confidence: 0.878341105833333

00:44:46.730 --> 00:44:48.746 And we're using a method called

NOTE Confidence: 0.878341105833333

00:44:48.750 --> 00:44:51.414 10X Vizio and what it does is you

NOTE Confidence: 0.878341105833333

00:44:51.414 --> 00:44:54.117 can see in this top left corner.

NOTE Confidence: 0.878341105833333

00:44:54.120 --> 00:44:55.840 This is a glass slide and you can

NOTE Confidence: 0.878341105833333

00:44:55.840 --> 00:44:57.976 put 4 slices of tissue on the slide,

NOTE Confidence: 0.878341105833333

00:44:57.980 --> 00:44:59.450 which is shown actually here.

NOTE Confidence: 0.878341105833333

00:44:59.450 --> 00:45:01.922 These are endomyocardial biopsies.

NOTE Confidence: 0.878341105833333

00:45:01.922 --> 00:45:04.394 And across those squares,

NOTE Confidence: 0.878341105833333

00:45:04.400 --> 00:45:06.480 there's like a barcode address

NOTE Confidence: 0.878341105833333

00:45:06.480 --> 00:45:09.339 for each 55 Micron core or space.

NOTE Confidence: 0.878341105833333

00:45:09.340 --> 00:45:10.666 And then the tissue that's put

NOTE Confidence: 0.878341105833333

00:45:10.666 --> 00:45:11.860 up on top of that,

NOTE Confidence: 0.878341105833333

00:45:11.860 --> 00:45:14.866 we identify what the RNAs are.

NOTE Confidence: 0.878341105833333

00:45:14.870 --> 00:45:15.207 They're,

NOTE Confidence: 0.878341105833333

00:45:15.207 --> 00:45:16.555 they're tagged with that

NOTE Confidence: 0.878341105833333

00:45:16.555 --> 00:45:18.240 barcode of where that's located

NOTE Confidence: 0.696277422142857

00:45:18.298 --> 00:45:19.698 and then they're sequenced.

NOTE Confidence: 0.696277422142857

00:45:19.700 --> 00:45:21.548 And so we know what the expression

NOTE Confidence: 0.696277422142857

00:45:21.548 --> 00:45:23.573 is in each one of those regions

NOTE Confidence: 0.696277422142857

00:45:23.573 --> 00:45:25.518 all the way across. The tissue.

NOTE Confidence: 0.696277422142857

00:45:25.518 --> 00:45:27.416 And so that's this particular

NOTE Confidence: 0.696277422142857

00:45:27.416 --> 00:45:28.908 type of spatial transcriptomics

NOTE Confidence: 0.696277422142857

00:45:28.908 --> 00:45:30.730 or other approaches as well.

NOTE Confidence: 0.696277422142857

00:45:30.730 --> 00:45:33.090 And I'm gonna stop for a second and

NOTE Confidence: 0.696277422142857

00:45:33.090 --> 00:45:35.787 get on my soapbox and say something.

NOTE Confidence: 0.696277422142857

00:45:35.790 --> 00:45:37.330 We as pathologists have got

NOTE Confidence: 0.696277422142857

00:45:37.330 --> 00:45:39.472 to get engaged in this concept

NOTE Confidence: 0.696277422142857

00:45:39.472 --> 00:45:41.089 of spatial transcriptomics.

NOTE Confidence: 0.696277422142857

00:45:41.090 --> 00:45:42.903 I am a member of the Human

NOTE Confidence: 0.696277422142857

00:45:42.903 --> 00:45:44.250 Cell Atlas and Hub map,

NOTE Confidence: 0.696277422142857

00:45:44.250 --> 00:45:46.538 which are two big NIH and other studies

NOTE Confidence: 0.696277422142857

00:45:46.538 --> 00:45:48.274 to identify where every cell is

NOTE Confidence: 0.696277422142857

00:45:48.274 --> 00:45:50.278 located in the human body and discover

NOTE Confidence: 0.696277422142857

00:45:50.278 --> 00:45:52.322 all the cell types and there are

NOTE Confidence: 0.696277422142857

00:45:52.322 --> 00:45:54.954 not enough pathologists in the room.

NOTE Confidence: 0.696277422142857

00:45:54.954 --> 00:45:56.998 These are brilliant bioinformaticians.

NOTE Confidence: 0.696277422142857

00:45:57.000 --> 00:45:58.272 They do great science.

NOTE Confidence: 0.696277422142857

00:45:58.272 --> 00:46:01.854 But a lot of them don't know 110th of what

NOTE Confidence: 0.696277422142857

00:46:01.854 --> 00:46:04.260 you guys intuitively know about tissue.

NOTE Confidence: 0.696277422142857

00:46:04.260 --> 00:46:06.790 And it would benefit all of them if we as

NOTE Confidence: 0.696277422142857

00:46:06.853 --> 00:46:09.197 a society or a group get more engaged,

NOTE Confidence: 0.696277422142857

00:46:09.200 --> 00:46:10.870 particularly now that they're starting

NOTE Confidence: 0.696277422142857

00:46:10.870 --> 00:46:12.540 to move to spatial transcriptomics

NOTE Confidence: 0.696277422142857

00:46:12.594 --> 00:46:13.739 and really need our help.

NOTE Confidence: 0.696277422142857

00:46:13.740 --> 00:46:15.756 Kevin, get off my soapbox now.

NOTE Confidence: 0.696277422142857

00:46:15.760 --> 00:46:17.552 But I had to say that I feel

NOTE Confidence: 0.696277422142857

00:46:17.552 --> 00:46:18.620 very passionate about that.

NOTE Confidence: 0.696277422142857

00:46:18.620 --> 00:46:20.083 I sometimes go to these meetings and

NOTE Confidence: 0.696277422142857

00:46:20.083 --> 00:46:21.779 I'm the only pathologist in the room,

NOTE Confidence: 0.696277422142857

00:46:21.780 --> 00:46:24.160 and I I often shake my head.

NOTE Confidence: 0.696277422142857

00:46:24.160 --> 00:46:25.420 OK, so but. Back to this.

NOTE Confidence: 0.696277422142857

00:46:25.420 --> 00:46:27.814 So we decided to use this approach

NOTE Confidence: 0.696277422142857

00:46:27.814 --> 00:46:29.380 now spatial this method,

NOTE Confidence: 0.696277422142857

00:46:29.380 --> 00:46:32.680 these core sizes are 55 microns,

NOTE Confidence: 0.696277422142857

00:46:32.680 --> 00:46:34.184 which is not the size of a cell.

NOTE Confidence: 0.696277422142857

00:46:34.190 --> 00:46:36.899 They're bigger than a normal small cell,

NOTE Confidence: 0.696277422142857

00:46:36.900 --> 00:46:39.420 but a cardiac myocyte is a big cell.

NOTE Confidence: 0.696277422142857

00:46:39.420 --> 00:46:42.140 So the match is pretty close to 1:00 to 1:00.

NOTE Confidence: 0.696277422142857

00:46:42.140 --> 00:46:45.020 So we feel good about that.

NOTE Confidence: 0.696277422142857

00:46:45.020 --> 00:46:46.020 You can see here though,

NOTE Confidence: 0.696277422142857

00:46:46.020 --> 00:46:47.376 these are endomyocardial biopsies

NOTE Confidence: 0.696277422142857

00:46:47.376 --> 00:46:49.071 after we've already used them

NOTE Confidence: 0.696277422142857

00:46:49.071 --> 00:46:50.379 for clinical purposes.

NOTE Confidence: 0.696277422142857

00:46:50.380 --> 00:46:52.460 So the amount of tissue left wasn't great,

NOTE Confidence: 0.696277422142857

00:46:52.460 --> 00:46:54.960 but for these are myocarditis.

NOTE Confidence: 0.696277422142857

00:46:54.960 --> 00:46:57.770 For these are non myocarditis.

NOTE Confidence: 0.696277422142857

00:46:57.770 --> 00:46:59.786 We we did this with a core facility

NOTE Confidence: 0.696277422142857

00:46:59.786 --> 00:47:01.302 at Hopkins. We generated some data.

NOTE Confidence: 0.696277422142857

00:47:01.302 --> 00:47:03.069 The first thing I always like to

NOTE Confidence: 0.696277422142857

00:47:03.069 --> 00:47:04.483 do with data is kick the tires,

NOTE Confidence: 0.696277422142857

00:47:04.490 --> 00:47:06.254 make sure that it seems reasonable and

NOTE Confidence: 0.696277422142857

00:47:06.254 --> 00:47:08.570 it actually did. I was pretty happy.

NOTE Confidence: 0.696277422142857

00:47:08.570 --> 00:47:10.520 These are two macrophage markers,

NOTE Confidence: 0.833239409166667

00:47:12.950 --> 00:47:14.360 CD74TSB4X and you can see

NOTE Confidence: 0.833239409166667

00:47:14.360 --> 00:47:16.250 where one was high in a core,

NOTE Confidence: 0.833239409166667

00:47:16.250 --> 00:47:17.307 the other was high in a core.

NOTE Confidence: 0.833239409166667

00:47:17.310 --> 00:47:19.170 Each one of these dots represents

NOTE Confidence: 0.833239409166667

00:47:19.170 --> 00:47:21.310 a core from across these tissues.

NOTE Confidence: 0.833239409166667

00:47:21.310 --> 00:47:23.575 These are two markers of

NOTE Confidence: 0.833239409166667

00:47:23.575 --> 00:47:25.387 cardiac myocytes tropomyosin 1,

NOTE Confidence: 0.833239409166667

00:47:25.390 --> 00:47:26.702 myosin light chain two.

NOTE Confidence: 0.833239409166667

00:47:26.702 --> 00:47:27.686 Again there was.

NOTE Confidence: 0.833239409166667

00:47:27.690 --> 00:47:29.061 Very strong correlation

NOTE Confidence: 0.833239409166667

00:47:29.061 --> 00:47:30.889 collagens for fibroblasts and

NOTE Confidence: 0.833239409166667

00:47:30.889 --> 00:47:33.080 hemoglobins for red blood cells.

NOTE Confidence: 0.833239409166667

00:47:33.080 --> 00:47:35.165 So this method actually worked

NOTE Confidence: 0.833239409166667

00:47:35.165 --> 00:47:36.833 reasonably well at identifying

NOTE Confidence: 0.833239409166667

00:47:36.833 --> 00:47:38.708 what was present at each of

NOTE Confidence: 0.833239409166667

00:47:38.708 --> 00:47:40.860 those cells and if we did a UMAP,

NOTE Confidence: 0.833239409166667

00:47:40.860 --> 00:47:43.730 which is a way of sort of

NOTE Confidence: 0.833239409166667

00:47:43.730 --> 00:47:45.320 structuring the data in.

NOTE Confidence: 0.833239409166667

00:47:45.320 --> 00:47:46.795 Kind of from A3 dimensional

NOTE Confidence: 0.833239409166667

00:47:46.795 --> 00:47:48.270 where everything is located down

NOTE Confidence: 0.833239409166667

00:47:48.323 --> 00:47:49.748 to two-dimensional structure.

NOTE Confidence: 0.833239409166667

00:47:49.750 --> 00:47:52.330 You can see that this separated

NOTE Confidence: 0.833239409166667

00:47:52.330 --> 00:47:54.050 the myocarditis cases from

NOTE Confidence: 0.833239409166667

00:47:54.130 --> 00:47:56.058 the non myocarditis cases.

NOTE Confidence: 0.833239409166667

00:47:56.060 --> 00:47:57.200 So the signal, the,

NOTE Confidence: 0.833239409166667

00:47:57.200 --> 00:47:59.239 the question we were asking though is

NOTE Confidence: 0.833239409166667

00:47:59.239 --> 00:48:01.157 can we see interesting signals at a

NOTE Confidence: 0.833239409166667

00:48:01.157 --> 00:48:02.980 distance from the inflammatory cells?

NOTE Confidence: 0.833239409166667

00:48:02.980 --> 00:48:04.793 Can we pick up something that the

NOTE Confidence: 0.833239409166667

00:48:04.793 --> 00:48:06.320 myocytes next door are screaming,

NOTE Confidence: 0.833239409166667

00:48:06.320 --> 00:48:07.060 hey, hey,

NOTE Confidence: 0.833239409166667

00:48:07.060 --> 00:48:08.540 I'm seeing there's this

NOTE Confidence: 0.833239409166667

00:48:08.540 --> 00:48:10.400 inflammation going on over here.

NOTE Confidence: 0.833239409166667

00:48:10.400 --> 00:48:12.900 And so this is just a little bit of data.

NOTE Confidence: 0.833239409166667

00:48:12.900 --> 00:48:14.514 My buddy Luigi thinks he's going

NOTE Confidence: 0.833239409166667

00:48:14.514 --> 00:48:16.400 to make a company make millions.

NOTE Confidence: 0.833239409166667

00:48:16.400 --> 00:48:17.324 I don't think so.

NOTE Confidence: 0.833239409166667

00:48:17.324 --> 00:48:19.396 But I told him I wouldn't tell him what

NOTE Confidence: 0.833239409166667

00:48:19.396 --> 00:48:21.460 a gene name was and so he was happy.

NOTE Confidence: 0.833239409166667

00:48:21.460 --> 00:48:23.914 So this is an example of

NOTE Confidence: 0.833239409166667

00:48:23.914 --> 00:48:25.550 of what we're seeing.

NOTE Confidence: 0.833239409166667

00:48:25.550 --> 00:48:27.503 This is a collection of immune cells

NOTE Confidence: 0.833239409166667

00:48:27.503 --> 00:48:29.580 right here on the edge of a biopsy.

NOTE Confidence: 0.833239409166667

00:48:29.580 --> 00:48:31.235 And you'll note there's not

NOTE Confidence: 0.833239409166667

00:48:31.235 --> 00:48:33.300 a blue or Gray signal here.

NOTE Confidence: 0.833239409166667

00:48:33.300 --> 00:48:36.184 What we've done is we've removed any

NOTE Confidence: 0.833239409166667

00:48:36.184 --> 00:48:40.516 location that had CD 45 positivity or PT PRC.

NOTE Confidence: 0.833239409166667

00:48:40.520 --> 00:48:42.616 CD 45 is a pan immune cell marker.

NOTE Confidence: 0.833239409166667

00:48:42.620 --> 00:48:45.374 So we said let's ignore anywhere

NOTE Confidence: 0.833239409166667

00:48:45.374 --> 00:48:47.710 where there's an immune cell.

NOTE Confidence: 0.833239409166667

00:48:47.710 --> 00:48:50.170 Then let's see what is present

NOTE Confidence: 0.833239409166667

00:48:50.170 --> 00:48:53.296 in myocarditis samples.

NOTE Confidence: 0.833239409166667

00:48:53.296 --> 00:48:55.380 In nonimmune.

NOTE Confidence: 0.833239409166667

00:48:55.380 --> 00:48:56.990 Help.

NOTE Confidence: 0.833239409166667

00:48:56.990 --> 00:48:59.910 Whole of one of the genes that was

NOTE Confidence: 0.833239409166667

00:48:59.910 --> 00:49:02.000 identified where each one of these

NOTE Confidence: 0.833239409166667

00:49:02.000 --> 00:49:04.720 blue dots has a signal from that gene.

NOTE Confidence: 0.833239409166667

00:49:04.720 --> 00:49:06.764 And every Gray area is a place

NOTE Confidence: 0.833239409166667

00:49:06.764 --> 00:49:09.054 where it doesn't and you can see

NOTE Confidence: 0.833239409166667

00:49:09.054 --> 00:49:10.398 across this myocarditis biopsy

NOTE Confidence: 0.833239409166667

00:49:10.398 --> 00:49:12.691 we have lots and lots of these

NOTE Confidence: 0.833239409166667

00:49:12.691 --> 00:49:14.786 blue signals versus here on this

NOTE Confidence: 0.833239409166667

00:49:14.786 --> 00:49:17.466 non myocarditis case we have

NOTE Confidence: 0.833239409166667

00:49:17.466 --> 00:49:19.731 almost no CD 45 positivity.

NOTE Confidence: 0.833239409166667

00:49:19.731 --> 00:49:22.510 We immune cells are rare in normal

NOTE Confidence: 0.833239409166667

00:49:22.595 --> 00:49:25.301 heart although they are present and

NOTE Confidence: 0.833239409166667

00:49:25.301 --> 00:49:28.178 just an occasional spot of this blue.

NOTE Confidence: 0.833239409166667

00:49:28.180 --> 00:49:30.172 So that to me is is pretty optimistic

NOTE Confidence: 0.833239409166667

00:49:30.172 --> 00:49:32.344 that we are seeing signals coming from

NOTE Confidence: 0.833239409166667

00:49:32.344 --> 00:49:34.690 non immune cells that could be doing

NOTE Confidence: 0.833239409166667

00:49:34.690 --> 00:49:36.730 exactly what we're hoping for signaling.

NOTE Confidence: 0.833239409166667

00:49:36.730 --> 00:49:39.850 That inflammation is nearby.

NOTE Confidence: 0.833239409166667

00:49:39.850 --> 00:49:42.050 This is a a more recently I was able to

NOTE Confidence: 0.833239409166667

00:49:42.110 --> 00:49:44.366 look at a case of a chronic myocarditis,

NOTE Confidence: 0.833239409166667

00:49:44.370 --> 00:49:46.806 lots of immune cells but without

NOTE Confidence: 0.833239409166667

00:49:46.806 --> 00:49:48.430 myocyte inflammation from a

NOTE Confidence: 0.833239409166667

00:49:48.498 --> 00:49:50.188 a larger chunk of tissue.

NOTE Confidence: 0.833239409166667

00:49:50.190 --> 00:49:52.826 And here again this is CD45 which

NOTE Confidence: 0.833239409166667

00:49:52.826 --> 00:49:54.866 are these cells right here.

NOTE Confidence: 0.833239409166667

00:49:54.870 --> 00:49:57.230 The adipocytes in this location

NOTE Confidence: 0.833239409166667

00:49:57.230 --> 00:49:59.590 are this stream right along

NOTE Confidence: 0.833239409166667

00:49:59.677 --> 00:50:02.078 the side and so where you see.

NOTE Confidence: 0.833239409166667

00:50:02.080 --> 00:50:04.048 There are are.

NOTE Confidence: 0.802991209090909

00:50:09.270 --> 00:50:11.178 The first was that there was

NOTE Confidence: 0.802991209090909

00:50:11.178 --> 00:50:13.120 actually like a negative biomarker.

NOTE Confidence: 0.771345498571429

00:50:16.340 --> 00:50:17.672 Have reasonable expression

NOTE Confidence: 0.771345498571429

00:50:17.672 --> 00:50:19.448 levels of this marker.

NOTE Confidence: 0.771345498571429

00:50:19.450 --> 00:50:21.736 And then as we got closer to the immune

NOTE Confidence: 0.771345498571429

00:50:21.736 --> 00:50:23.186 infiltrate, which was over here,

NOTE Confidence: 0.771345498571429

00:50:23.186 --> 00:50:25.873 we started to see less of that biomarker

NOTE Confidence: 0.771345498571429

00:50:25.873 --> 00:50:28.357 and we also had positive biomarkers.

NOTE Confidence: 0.771345498571429

00:50:28.360 --> 00:50:30.200 So again, CD45 represents

NOTE Confidence: 0.771345498571429

00:50:30.200 --> 00:50:32.040 all the immune cells.

NOTE Confidence: 0.771345498571429

00:50:32.040 --> 00:50:34.418 If we go beyond that, you start to

NOTE Confidence: 0.771345498571429

00:50:34.418 --> 00:50:36.398 seeing there's more signal there.

NOTE Confidence: 0.771345498571429

00:50:36.400 --> 00:50:38.284 So we are somewhat optimistic we

NOTE Confidence: 0.771345498571429

00:50:38.284 --> 00:50:40.683 might be able to find something that

NOTE Confidence: 0.771345498571429

00:50:40.683 --> 00:50:43.196 will extend out from areas of injury

NOTE Confidence: 0.771345498571429

00:50:43.260 --> 00:50:45.440 and that can identify myocarditis.

NOTE Confidence: 0.771345498571429

00:50:45.440 --> 00:50:46.472 And I'll add that we're not

NOTE Confidence: 0.771345498571429

00:50:46.472 --> 00:50:47.380 the only people doing this,

NOTE Confidence: 0.771345498571429

00:50:47.380 --> 00:50:47.989 I've already heard.

NOTE Confidence: 0.771345498571429

00:50:47.989 --> 00:50:49.840 Of lots of other groups have had this idea.

NOTE Confidence: 0.771345498571429

00:50:49.840 --> 00:50:50.938 I don't think we're that clever.

NOTE Confidence: 0.79585944

00:50:55.080 --> 00:50:56.280 But as I said before,

NOTE Confidence: 0.79585944

00:50:56.280 --> 00:50:58.260 the goals are to identify biomarkers

NOTE Confidence: 0.79585944

00:50:58.260 --> 00:51:00.899 or a biomarker that can be used to

NOTE Confidence: 0.79585944

00:51:00.899 --> 00:51:02.464 diagnose myocarditis in the absence

NOTE Confidence: 0.79585944

00:51:02.464 --> 00:51:04.437 of inflammation or myocyte injury

NOTE Confidence: 0.79585944

00:51:04.437 --> 00:51:06.437 in the right clinical setting.

NOTE Confidence: 0.79585944

00:51:06.440 --> 00:51:09.038 And ultimately the goal is to

NOTE Confidence: 0.79585944

00:51:09.038 --> 00:51:11.970 increase the yield on our biopsies.

NOTE Confidence: 0.79585944

00:51:11.970 --> 00:51:14.708 So I'm going to end things now and

NOTE Confidence: 0.79585944

00:51:14.708 --> 00:51:17.046 give you a few take home messages.

NOTE Confidence: 0.79585944

00:51:17.050 --> 00:51:19.468 There are challenges as I said,

NOTE Confidence: 0.79585944

00:51:19.470 --> 00:51:21.262 how to diagnose myocarditis

NOTE Confidence: 0.79585944

00:51:21.262 --> 00:51:25.253 in 2022 remains in. Oh.

NOTE Confidence: 0.79585944

00:51:25.253 --> 00:51:27.868 Don't have a great way

NOTE Confidence: 0.79585944

00:51:27.868 --> 00:51:29.960 of making the diagnosis.

NOTE Confidence: 0.79585944

00:51:29.960 --> 00:51:31.600 Biopsying which has historically

NOTE Confidence: 0.79585944

00:51:31.600 --> 00:51:33.650 been called the gold standard

NOTE Confidence: 0.79585944

00:51:33.650 --> 00:51:35.471 is plagued by inconsistencies

NOTE Confidence: 0.79585944

00:51:35.471 --> 00:51:37.716 how we approach the diagnosis,

NOTE Confidence: 0.79585944

00:51:37.720 --> 00:51:39.750 whether we can agree on the diagnosis

NOTE Confidence: 0.79585944

00:51:39.750 --> 00:51:41.616 and whether we can even see the

NOTE Confidence: 0.79585944

00:51:41.616 --> 00:51:43.640 areas we need to make the diagnosis.

NOTE Confidence: 0.79585944

00:51:43.640 --> 00:51:45.065 But there are also opportunities

NOTE Confidence: 0.79585944

00:51:45.065 --> 00:51:47.339 we are going to be working towards

NOTE Confidence: 0.79585944

00:51:47.339 --> 00:51:49.299 improved and new myocarditis criteria

NOTE Confidence: 0.79585944

00:51:49.299 --> 00:51:51.173 for biopsies and whole hearts

NOTE Confidence: 0.79585944

00:51:51.173 --> 00:51:53.087 which should improve the way we

NOTE Confidence: 0.79585944

00:51:53.087 --> 00:51:55.550 approach the biopsies and we think

NOTE Confidence: 0.79585944

00:51:55.550 --> 00:51:57.825 that non immune cell signaling.

NOTE Confidence: 0.79585944

00:51:57.830 --> 00:52:00.956 On biopsy can indicate myocarditis occurring

NOTE Confidence: 0.79585944

00:52:00.956 --> 00:52:05.097 even if we can't see those immune cells.

NOTE Confidence: 0.79585944

00:52:05.100 --> 00:52:07.130 So I want to thank Zen Liu for the work

NOTE Confidence: 0.79585944

00:52:07.191 --> 00:52:09.223 he did when we worked with our experts,

NOTE Confidence: 0.79585944

00:52:09.230 --> 00:52:11.430 Luigi and Kevin on the last part of

NOTE Confidence: 0.79585944

00:52:11.430 --> 00:52:13.198 this with the spatial transcriptomics

NOTE Confidence: 0.79585944

00:52:13.198 --> 00:52:15.893 and then members of our society and

NOTE Confidence: 0.79585944

00:52:15.957 --> 00:52:17.882 the European Society for working

NOTE Confidence: 0.79585944

00:52:17.882 --> 00:52:19.807 to update and create criteria.

NOTE Confidence: 0.79585944

00:52:19.810 --> 00:52:21.231 And I'll end there and I'm happy

NOTE Confidence: 0.79585944

00:52:21.231 --> 00:52:22.720 to take any of your questions.

NOTE Confidence: 0.5214029

00:52:31.690 --> 00:52:34.020 This question. Yeah.

NOTE Confidence: 0.63493805

00:52:36.480 --> 00:52:36.980 Look at.

NOTE Confidence: 0.9188627

00:52:43.230 --> 00:52:45.666 Yeah. So the the question from home,

NOTE Confidence: 0.794872648

00:52:45.670 --> 00:52:46.678 if I make sure I'm getting

NOTE Confidence: 0.794872648

00:52:46.678 --> 00:52:47.350 this right as well,

NOTE Confidence: 0.794872648

00:52:47.350 --> 00:52:50.982 is people looked at CD3 and how that

NOTE Confidence: 0.794872648

00:52:50.982 --> 00:52:54.888 relates to steroid use immunosuppression.

NOTE Confidence: 0.794872648

00:52:54.890 --> 00:52:57.210 So I don't know that I've seen that.

NOTE Confidence: 0.794872648

00:52:57.210 --> 00:52:58.730 I haven't done that,

NOTE Confidence: 0.794872648

00:52:58.730 --> 00:53:01.010 I'll tell you that right now.

NOTE Confidence: 0.794872648

00:53:01.010 --> 00:53:02.630 And I have to look there,

NOTE Confidence: 0.794872648

00:53:02.630 --> 00:53:04.240 that's going to be one of the

NOTE Confidence: 0.794872648

00:53:04.240 --> 00:53:05.439 huge challenges that we're going

NOTE Confidence: 0.794872648

00:53:05.439 --> 00:53:07.049 to face when we try and evaluate

NOTE Confidence: 0.794872648

00:53:07.049 --> 00:53:08.707 these is what are the different

NOTE Confidence: 0.794872648

00:53:08.707 --> 00:53:10.087 treatments that patients have had,

NOTE Confidence: 0.794872648

00:53:10.090 --> 00:53:11.845 because that's going to impact

NOTE Confidence: 0.794872648

00:53:11.845 --> 00:53:13.535 on outcome as well, right.

NOTE Confidence: 0.794872648

00:53:13.535 --> 00:53:15.815 So normally at a time of biopsy early

NOTE Confidence: 0.794872648

00:53:15.815 --> 00:53:18.308 when we're diagnosed as acute myocarditis,

NOTE Confidence: 0.794872648

00:53:18.310 --> 00:53:19.090 they haven't necessarily

NOTE Confidence: 0.794872648

00:53:19.090 --> 00:53:20.390 gone on a treatment yet.

NOTE Confidence: 0.794872648

00:53:20.390 --> 00:53:23.846 So what we see is really more natively

NOTE Confidence: 0.794872648

00:53:23.846 --> 00:53:25.820 what's happening in the heart.

NOTE Confidence: 0.794872648

00:53:25.820 --> 00:53:27.872 So we could see the full

NOTE Confidence: 0.794872648

00:53:27.872 --> 00:53:29.240 gamut of inflammation there,

NOTE Confidence: 0.794872648

00:53:29.240 --> 00:53:32.222 but the question is if different practices

NOTE Confidence: 0.794872648

00:53:32.222 --> 00:53:34.325 and different institutions treat with

NOTE Confidence: 0.794872648

00:53:34.325 --> 00:53:36.593 steroids or don't treat with steroids,

NOTE Confidence: 0.794872648

00:53:36.600 --> 00:53:39.360 how do we figure that out for outcome?

NOTE Confidence: 0.794872648

00:53:39.360 --> 00:53:41.138 And that's a good question as well.

NOTE Confidence: 0.794872648

00:53:41.140 --> 00:53:43.390 And that's going to be very hard to do

NOTE Confidence: 0.794872648

00:53:43.390 --> 00:53:45.407 where we're going to look at different

NOTE Confidence: 0.794872648

00:53:45.407 --> 00:53:47.518 data sets and and figure that out.

NOTE Confidence: 0.794872648

00:53:47.520 --> 00:53:49.370 Second question,

NOTE Confidence: 0.794872648

00:53:49.370 --> 00:53:49.870 yes.

NOTE Confidence: 0.543855205

00:53:51.420 --> 00:53:54.180 That was something against

NOTE Confidence: 0.543855205

00:53:54.180 --> 00:53:56.590 what people think or.

NOTE Confidence: 0.871884275714286

00:53:57.770 --> 00:54:01.250 Yeah, I, I I don't remember anymore. I.

NOTE Confidence: 0.18045843

00:54:16.260 --> 00:54:16.750 Today.

NOTE Confidence: 0.687088440714286

00:54:21.190 --> 00:54:26.182 My question is how expanded would be these

NOTE Confidence: 0.687088440714286

00:54:26.182 --> 00:54:30.177 changes around the areas or permission?

NOTE Confidence: 0.687088440714286

00:54:30.180 --> 00:54:32.310 Because if it is really expanded

NOTE Confidence: 0.687088440714286

00:54:32.310 --> 00:54:34.530 then you would have a higher

NOTE Confidence: 0.687088440714286

00:54:34.530 --> 00:54:36.335 chance of violating for each

NOTE Confidence: 0.687088440714286

00:54:36.340 --> 00:54:40.740 and every other piece but.

NOTE Confidence: 0.687088440714286

00:54:40.740 --> 00:54:43.210 Yeah, and you will stop.

NOTE Confidence: 0.687088440714286

00:54:43.210 --> 00:54:44.706 Basically the same time

NOTE Confidence: 0.687088440714286

00:54:44.706 --> 00:54:46.576 concept of meeting the area.

NOTE Confidence: 0.804246022857143

00:54:47.930 --> 00:54:50.642 Yeah, you, you exactly elucidate the

NOTE Confidence: 0.804246022857143

00:54:50.642 --> 00:54:53.807 the question that we have no idea of,

NOTE Confidence: 0.804246022857143

00:54:53.810 --> 00:54:56.802 which is how far out will that signal

NOTE Confidence: 0.804246022857143

00:54:56.802 --> 00:54:58.609 extend relative to the biopsy.

NOTE Confidence: 0.804246022857143

00:54:58.610 --> 00:55:00.866 And the longer, the further out it goes,

NOTE Confidence: 0.804246022857143

00:55:00.870 --> 00:55:02.676 the more successful this is going

NOTE Confidence: 0.804246022857143

00:55:02.676 --> 00:55:05.228 to be and the less it extends out,

NOTE Confidence: 0.804246022857143

00:55:05.230 --> 00:55:06.749 the less successful it's going to be.

NOTE Confidence: 0.804246022857143

00:55:06.750 --> 00:55:09.945 And we've only shown we've only done this on.

NOTE Confidence: 0.804246022857143

00:55:09.950 --> 00:55:11.678 5 myocarditis cases for

NOTE Confidence: 0.804246022857143

00:55:11.678 --> 00:55:13.406 acute and one chronic.

NOTE Confidence: 0.804246022857143

00:55:13.410 --> 00:55:16.110 We've put in some grants to try and get many,

NOTE Confidence: 0.804246022857143

00:55:16.110 --> 00:55:17.840 many more cases and find

NOTE Confidence: 0.804246022857143

00:55:17.840 --> 00:55:19.570 the markers that have the,

NOTE Confidence: 0.804246022857143

00:55:19.570 --> 00:55:22.244 the sort of the widest capture area.

NOTE Confidence: 0.804246022857143

00:55:22.250 --> 00:55:23.734 And that's going to be absolutely critical.

NOTE Confidence: 0.804246022857143

00:55:23.740 --> 00:55:25.126 And if we don't find anything,

NOTE Confidence: 0.804246022857143

00:55:25.130 --> 00:55:26.738 this obviously won't work.

NOTE Confidence: 0.804246022857143

00:55:26.738 --> 00:55:28.642 So high risk, high reward,

NOTE Confidence: 0.804246022857143

00:55:28.642 --> 00:55:31.064 but if we can't extend that out,

NOTE Confidence: 0.804246022857143

00:55:31.070 --> 00:55:32.335 we're going to be able

NOTE Confidence: 0.804246022857143

00:55:32.335 --> 00:55:33.347 to make more diagnosis.

NOTE Confidence: 0.804246022857143

00:55:33.350 --> 00:55:34.771 And I think that's a great thing

NOTE Confidence: 0.804246022857143

00:55:34.771 --> 00:55:36.219 that we can make that happen.

NOTE Confidence: 0.8564615

00:55:38.960 --> 00:55:42.798 So I just. Questions why is the?

NOTE Confidence: 0.646198923333333

00:55:48.640 --> 00:55:50.050 So that and we stop typing.

NOTE Confidence: 0.23320433

00:55:52.130 --> 00:55:52.680 Tell.

NOTE Confidence: 0.42452544

00:55:55.220 --> 00:55:55.600 Weather.

NOTE Confidence: 0.95544696

00:55:58.820 --> 00:56:00.860 Yeah, so that's a great question.

NOTE Confidence: 0.741508418333333

00:56:00.860 --> 00:56:03.830 Do we do subtyping of CD3?

NOTE Confidence: 0.741508418333333

00:56:03.830 --> 00:56:06.310 We do not. So one of the the I think

NOTE Confidence: 0.741508418333333

00:56:06.384 --> 00:56:08.316 challenges in the cardiovascular

NOTE Confidence: 0.741508418333333

00:56:08.316 --> 00:56:11.510 pathology space is that we have not

NOTE Confidence: 0.741508418333333

00:56:11.510 --> 00:56:14.450 really kept up in our field with.

NOTE Confidence: 0.741508418333333

00:56:14.450 --> 00:56:16.490 Things like this like subtyping CD3

NOTE Confidence: 0.741508418333333

00:56:16.490 --> 00:56:19.359 cells I on the research side it may

NOTE Confidence: 0.741508418333333

00:56:19.359 --> 00:56:21.989 have happened but most people in the

NOTE Confidence: 0.741508418333333

00:56:21.989 --> 00:56:24.761 cardiovascular space just use CD3 and CD68.

NOTE Confidence: 0.741508418333333

00:56:24.761 --> 00:56:27.428 In fact this came up last week

NOTE Confidence: 0.741508418333333

00:56:27.430 --> 00:56:29.056 when Peter had a journal club.

NOTE Confidence: 0.741508418333333

00:56:29.060 --> 00:56:31.811 When we're talking about C 68 positive

NOTE Confidence: 0.741508418333333

00:56:31.811 --> 00:56:33.720 cells were being increased seen in

NOTE Confidence: 0.741508418333333

00:56:33.720 --> 00:56:35.563 COVID and our colleague Jeff Zaffis

NOTE Confidence: 0.741508418333333

00:56:35.563 --> 00:56:37.488 was arguing that it's it's silly to

NOTE Confidence: 0.741508418333333

00:56:37.488 --> 00:56:39.920 just look at CD 68 that we have to

NOTE Confidence: 0.741508418333333

00:56:39.920 --> 00:56:41.238 sub classify macrophages because we

NOTE Confidence: 0.741508418333333

00:56:41.238 --> 00:56:42.852 know there's so many phenotypes of

NOTE Confidence: 0.741508418333333

00:56:42.852 --> 00:56:44.358 macrophages that's really meaningful but.

NOTE Confidence: 0.741508418333333

00:56:44.360 --> 00:56:46.264 They don't have the tool to do that

NOTE Confidence: 0.741508418333333

00:56:46.264 --> 00:56:48.509 and we just haven't implemented them.

NOTE Confidence: 0.741508418333333

00:56:48.510 --> 00:56:51.390 So we don't go beyond CD3.

NOTE Confidence: 0.741508418333333

00:56:51.390 --> 00:56:51.974 Should we?

NOTE Confidence: 0.741508418333333

00:56:51.974 --> 00:56:54.018 Yes, I mentioned TH 17 cells seem

NOTE Confidence: 0.741508418333333

00:56:54.018 --> 00:56:55.790 to be important in myocarditis

NOTE Confidence: 0.741508418333333

00:56:55.790 --> 00:56:57.914 and we are not doing anything

NOTE Confidence: 0.741508418333333

00:56:57.980 --> 00:57:00.278 clinically to chase that down either.

NOTE Confidence: 0.2796874

00:57:04.990 --> 00:57:05.680 Exactly.

NOTE Confidence: 0.659317546363636

00:57:10.430 --> 00:57:13.088 And ideas? So only small factory

NOTE Confidence: 0.659317546363636

00:57:13.088 --> 00:57:15.370 of people would have this.

NOTE Confidence: 0.780528216666667

00:57:20.730 --> 00:57:23.370 So once you know what possible,

NOTE Confidence: 0.780528216666667

00:57:23.370 --> 00:57:25.770 you know what you think is

NOTE Confidence: 0.780528216666667

00:57:25.770 --> 00:57:28.828 underlying, you know, facts.

NOTE Confidence: 0.780528216666667

00:57:28.830 --> 00:57:32.468 This small. Right, so you know.

NOTE Confidence: 0.48627472

00:57:34.530 --> 00:57:34.860 Out.

NOTE Confidence: 0.741980668571429

00:57:36.540 --> 00:57:38.804 Got it. Yeah. So the question is why

NOTE Confidence: 0.741980668571429

00:57:38.804 --> 00:57:41.057 does these small group have Microsoft?

NOTE Confidence: 0.741980668571429

00:57:41.060 --> 00:57:42.210 I thought you were gonna ask, well,

NOTE Confidence: 0.741980668571429

00:57:42.210 --> 00:57:43.820 why are so many people have cardiac

NOTE Confidence: 0.741980668571429

00:57:43.820 --> 00:57:44.800 symptoms without myocarditis,

NOTE Confidence: 0.741980668571429

00:57:44.800 --> 00:57:46.180 which to me is easier.

NOTE Confidence: 0.741980668571429

00:57:46.180 --> 00:57:49.060 We're seeing small vessel a thrombi,

NOTE Confidence: 0.741980668571429

00:57:49.060 --> 00:57:50.736 microthrombi in in people.

NOTE Confidence: 0.741980668571429

00:57:50.736 --> 00:57:52.831 We're seeing increased macrophages in

NOTE Confidence: 0.741980668571429

00:57:52.831 --> 00:57:55.479 the hearts of multiple studies of that.

NOTE Confidence: 0.741980668571429

00:57:55.480 --> 00:57:57.080 But that's not myocarditis,

NOTE Confidence: 0.741980668571429

00:57:57.080 --> 00:57:58.680 that's just other processes

NOTE Confidence: 0.741980668571429

00:57:58.680 --> 00:58:00.799 that are affecting the heart.

NOTE Confidence: 0.741980668571429

00:58:00.800 --> 00:58:02.540 As far as this group,

NOTE Confidence: 0.741980668571429

00:58:02.540 --> 00:58:06.334 I don't know why this 2% I would argue.

NOTE Confidence: 0.741980668571429

00:58:06.334 --> 00:58:07.846 Genetics is partly involved.

NOTE Confidence: 0.741980668571429

00:58:07.850 --> 00:58:12.330 Someone's set up for this, possibly.

NOTE Confidence: 0.741980668571429

00:58:12.330 --> 00:58:13.770 Sort of an autoimmune process

NOTE Confidence: 0.741980668571429

00:58:13.770 --> 00:58:15.550 that can get going as well.

NOTE Confidence: 0.741980668571429

00:58:15.550 --> 00:58:18.042 I have not kept up with the

NOTE Confidence: 0.741980668571429

00:58:18.042 --> 00:58:19.810 basic science data on this.

NOTE Confidence: 0.741980668571429

00:58:19.810 --> 00:58:21.370 I'm sure there is a,

NOTE Confidence: 0.741980668571429

00:58:21.370 --> 00:58:22.648 I'm sure there's hundreds of papers.

NOTE Confidence: 0.741980668571429

00:58:22.650 --> 00:58:24.370 Whether some of them are good or not,

NOTE Confidence: 0.741980668571429

00:58:24.370 --> 00:58:25.630 I don't know either.

NOTE Confidence: 0.741980668571429

00:58:25.630 --> 00:58:28.010 But what we do know from COVID,

NOTE Confidence: 0.741980668571429

00:58:28.010 --> 00:58:29.410 having looked at lots of

NOTE Confidence: 0.741980668571429

00:58:29.410 --> 00:58:30.810 cases I'm sure Peter agrees,

NOTE Confidence: 0.741980668571429

00:58:30.810 --> 00:58:32.688 is we see lots of macrophages,

NOTE Confidence: 0.741980668571429

00:58:32.690 --> 00:58:35.000 I even see more macrophages and people

NOTE Confidence: 0.741980668571429

00:58:35.000 --> 00:58:37.449 have heart failure after getting a vaccine,

NOTE Confidence: 0.741980668571429

00:58:37.450 --> 00:58:39.452 but it's not a classic myocarditis and

NOTE Confidence: 0.741980668571429

00:58:39.452 --> 00:58:40.934 that's actually something that we're

NOTE Confidence: 0.741980668571429

00:58:40.934 --> 00:58:42.644 thinking about with the Dallas criteria.

NOTE Confidence: 0.741980668571429

00:58:42.650 --> 00:58:43.787 Is do we?

NOTE Confidence: 0.741980668571429

00:58:43.787 --> 00:58:46.440 Discussed some of these rare types of

NOTE Confidence: 0.741980668571429

00:58:46.527 --> 00:58:48.987 myocarditis and be provide criteria

NOTE Confidence: 0.741980668571429

00:58:48.987 --> 00:58:51.898 that are more specific to them

NOTE Confidence: 0.741980668571429

00:58:51.898 --> 00:58:54.802 such as if you see this many miles

NOTE Confidence: 0.741980668571429

00:58:54.802 --> 00:58:56.731 sites and I've seen a ton of Maya

NOTE Confidence: 0.741980668571429

00:58:56.731 --> 00:58:58.757 sites in a couple of these cases,

NOTE Confidence: 0.741980668571429

00:58:58.760 --> 00:59:00.488 but that's not typical for myocarditis

NOTE Confidence: 0.741980668571429

00:59:00.488 --> 00:59:02.070 which is a lymphocytic disease.

NOTE Confidence: 0.741980668571429

00:59:02.070 --> 00:59:03.380 We've always thought about whether

NOTE Confidence: 0.741980668571429

00:59:03.380 --> 00:59:05.383 or not that should be sufficient to

NOTE Confidence: 0.741980668571429

00:59:05.383 --> 00:59:06.988 make the diagnosis of myocarditis.

NOTE Confidence: 0.741980668571429

00:59:06.990 --> 00:59:09.495 So that's something that we're

NOTE Confidence: 0.741980668571429

00:59:09.495 --> 00:59:11.499 working through as well.

NOTE Confidence: 0.741980668571429

00:59:11.500 --> 00:59:12.090 After that.

NOTE Confidence: 0.53410596

00:59:16.950 --> 00:59:17.460 Ohh.

NOTE Confidence: 0.8311198

00:59:20.310 --> 00:59:21.999 We have talked about smoking in

NOTE Confidence: 0.8311198

00:59:21.999 --> 00:59:24.297 the smoking nut in the mice,

NOTE Confidence: 0.68932998

00:59:24.310 --> 00:59:26.870 which they activate phase

NOTE Confidence: 0.68932998

00:59:26.870 --> 00:59:31.549 two and one. So that made.

NOTE Confidence: 0.6374205

00:59:33.870 --> 00:59:34.150 Now.

NOTE Confidence: 0.011551678

00:59:37.840 --> 00:59:39.010 Subpopulation.

NOTE Confidence: 0.7412228225

00:59:41.660 --> 00:59:42.580 So that will be.

NOTE Confidence: 0.614373583333333

00:59:46.300 --> 00:59:51.830 No, only one. Yeah, yeah, yeah.

NOTE Confidence: 0.3847024

00:59:53.990 --> 00:59:54.350 Favorite.

NOTE Confidence: 0.881277718

01:00:02.760 --> 01:00:03.990 You heard it here first.

NOTE Confidence: 0.88967291

01:00:08.750 --> 01:00:10.948 Yeah. Super fresh. Thank you for sharing.

NOTE Confidence: 0.85017335

01:00:12.940 --> 01:00:13.160 Yeah.

NOTE Confidence: 0.92597055

01:00:16.460 --> 01:00:18.730 Great. Well, with that, I think

NOTE Confidence: 0.92597055

01:00:18.730 --> 01:00:20.639 I'll thank you all for your time.

NOTE Confidence: 0.565841106666667

01:00:20.640 --> 01:00:23.100 It's been wonderful. Thank you.

NOTE Confidence: 0.6070799

01:00:27.610 --> 01:00:28.740 There was nothing in the chat.

NOTE Confidence: 0.28563768

01:00:34.920 --> 01:00:36.786 There's some studies in the machine learning.

NOTE Confidence: 0.42934057

01:00:39.940 --> 01:00:42.240 Reason.